

Civil Liberties of Scientists

On December 30, 1947 the AAAS Council passed a resolution instructing the President of the Association to appoint a Special Committee on Civil Liberties for Scientists. Maurice B. Visscher was named chairman, and with Philip Bard, Robert E. Cushman, Richard L. Meier, and James R. Newmen as members, and Walter Gellhorn as consultant, the Committee completed its investigations and submitted a 77-page report of findings and recommendations in December 1948. The full text

was referred to the Council, which voted by an overwhelming majority to publicize the findings, and it is planned ultimately to make the complete report available at cost to those who want access to it. Announcement will be made in Science when Maurice B. Visscher and E. C. Stakman have concluded editorial revisions and the report is ready for distribution. Meanwhile, by vote of the Executive Committee at its meeting July 7, the conclusions and recommendations are published herewith.

THERE IS AT PRESENT a tendency in public thinking to relate scientific activity almost wholly to military activity, exposing scientists more than most occupational groups to sustained and stringent limitations upon their professional freedom. Fearful lest these limitations exceed justifiable bounds, jeopardize the national welfare, and infringe the rights of scientists, the American Association for the Advancement of Science, in December 1947, created a Special Committee on the Civil Liberties of Scientists.

The present report embodies its conclusions and recommendations with respect to three main areas:

1. Restrictions on research and scientific information;
2. Measures to assure the personal reliability of scientists having access to confidential data;
3. Inquiries relating to the "loyalty" of scientific workers in federal employment.

CONCLUSIONS

I

Secrecy is damaging to both science and democracy. In both, progress and the detection of error depend upon open discussion and free interchange of ideas among widely divergent and widely separated groups.

Yet today, in the United States, we have within the body of science large regions of secrecy. We endorse the statement of the President's Scientific Research Board, which in its 1947 Report on Science and Public Policy said: "Strict military security in the narrow sense is not entirely consistent with the broader requirements of national security. To be secure as a Nation we must maintain a climate conducive to the full flowering of free inquiry. However important secrecy about military weapons may be, the fundamental discoveries of researchers must circulate freely to have full beneficial effect. . . . Security regulations, therefore, should be applied only when strictly neces-

sary and then limited to specific instruments, machines or processes. They should not attempt to cover basic principles of fundamental knowledge."

II

No matter how the area of secrecy may be delimited, there will undoubtedly remain some matters of scientific cognizance which should be kept confidential. So long as national policy dictates that secrecy be observed, the reliability of persons to whom these matters are entrusted must be assured; hence inquiries into the character and attitudes of these persons are warranted.

If national as well as individual interests are to be protected, however, improvements must be achieved in the policies and procedures of our present security clearance programs as they affect scientists who will be entrusted with classified information.

The Atomic Energy Commission and the National Military Establishment are the chief agencies concerned with the trustworthiness of scientists who have access to "restricted" or "classified" data. Neither of these agencies furnishes the affected scientist any statement of the reasoning underlying a conclusion which is adverse to him; neither one sets forth charges in a precisely formulated fashion; neither one requires that testimony used against an individual be made known to him, or that even casual and non-official informants be identified and produced for examination; neither one provides for the making of specific findings of fact; neither one undertakes to record and publish its opinions in a way which makes possible any public understanding or analysis of the determinations made.

In some respects the procedures of the Atomic Energy Commission are more fully elaborated than those of the National Military Establishment, though the military clearance of the latter may affect literally millions of employees of private industry engaged in the planning or production of articles for military

use. A military determination that clearance should not be granted a civilian scientist is subject to appeal to the Industrial Employment Review Board (IERB), composed of Army, Navy, and Air Force officers. Proceedings of the IERB are themselves "classified," which means that even the immediately affected employee is forbidden to discuss them, keep notes about the handling of his own case, or possess a copy of the record of the hearing. Despite the fact that its decisions have a drastically important impact upon the lives and careers of civilians entirely outside the public service, the tribunal is exclusively military in its composition and there is no opportunity for review of its judgments by an appellate body differently constituted. Such subjection of the destinies of civilians to military tribunals is contrary to national tradition. Quite apart from procedural inadequacies, the present organization for deciding security clearance cases is open to basic criticism.

The Atomic Energy Commission has recently manifested a tendency to require security clearance not only for those scientists who themselves have access to restricted data, but also for their fellow scientists with whom they may have personal contact. This is graver in its implications than even the serious procedural and administrative imperfections already noted. At Brookhaven National Laboratory, for example, where only perhaps one-tenth of the scientific personnel works within the area of secrecy, all scientists must be cleared as a condition of employment. This apparently reflects a yielding to uninformed or sensationalist legislators and others who tend to exaggerate the problem of "keeping our atomic secrets." The effect of the excessive precautions is to discourage participation in important research activities closely linked to the nation's well-being. Scientists are increasingly reluctant to commit their personal and professional reputations to those who have brought frivolous charges against respected colleagues. Moreover, the delays and expense often involved in obtaining security clearance deter qualified persons from entering the atomic energy program.

So far as disclosures of evidence reveal, the problem of faithless scientific personnel in this country appears to be markedly less grave than the public has been led to suppose. Moreover, informed scientists are in broad agreement that restricted data cannot be readily transmitted to unauthorized persons. In the circumstances which exist rather than those which are fancied to exist, the stringent application of personnel security clearance should be limited to smaller numbers of scientists rather than extended to ever larger groups. If nothing is done to reverse the present trend to require security clearance of scien-

tists who do not have or desire to have access to restricted data, it is likely that many of the most penetrating and original scientific minds will be turned to pursuits unrelated to further development of the atomic energy program. Work in that field will be shunned by men of ability and pride if they are constantly treated as objects of suspicion and possible calumny.

III

Executive Order No. 9835 provides that no person shall be employed in a federal post if he is believed to be disloyal to the government of the United States. This Loyalty Order does not supplant existing provisions for summary removal of employees on security grounds. Entirely without reference to security considerations, the Order seeks to assure "complete and unswerving loyalty to the United States" on the part of all those who are in its service.

No one doubts the importance of faithful discharge of duty by public officials. No one questions the propriety of the government's demanding that its employees be loyal to their jobs and to the democratic institutions they serve. The Loyalty Order is, however, basically objectionable because it seeks to determine the employee's loyalty by inquiring into his supposed thoughts and attitudes, which are established in large part by imputing to him the beliefs of his associates.

If the Loyalty Order is to be retained, a drastic revision is essential. Instead of focusing on an employee's associations, it should focus on his behavior in overt acts. Legislation already on the statute books amply protects the federal service against retention of employees who advocate overthrow of the government.

Insofar as the Loyalty Order purports to deal with such matters as espionage, sabotage, and disregard of instructions, it is wholly superfluous, since conduct of that character is not only criminal but is also fully subject to administrative disciplinary action under existing law and regulations. The failure to confine the Loyalty Order to matters of objective proof has engendered a feeling of insecurity in public employment and may be expected to lessen the vigorous intellectual independence which is a prime condition of sound scientific work as it is of an imaginative civil service. "Experimentation there may be in many things of deep concern," Judge Cardozo once wrote "but not in setting boundaries to thought, for thought freely communicated is the indispensable condition of intelligent experimentation, the one test of its validity." Unless there is elimination of the Order, the present emphasis on attitude rather than conduct, the

tion will suffer heavily from the present loyalty program.

Even if the Loyalty Order were to be continued without revision of its underlying philosophy, important changes in administrative methods are urgently needed. The present loyalty boards discharge simultaneously the functions of advocacy and adjudication. The content of the charges they issue and the conduct of the proceedings over which they preside do not assure that the facts and their implications will be fully explored. The organizations with which an employee may be identified are finally and conclusively characterized by the Attorney General without either the employee's or the organization's having any opportunity whatsoever to establish that the Attorney General was not fully informed. These and other procedural deficiencies can be corrected readily. So long as they remain, they accentuate the possibility of error in the loyalty program.

The fundamental shortcomings in the Loyalty Order, however, are not procedural. Rather, they are to be found in the very conceptions which the Order expresses. Refinement of administrative methods and gentility of official behavior are important, to be sure. But they are not basic. Until the Loyalty Order deals with the way employees act, rather than with the way they supposedly think, we shall inhibit the freedom and encourage the insecurity of our public servants. The cost will in the end be borne not by the employees who are deprived of their normal freedom to believe and behave as they wish within the limits law has set. It will be borne by the nation as a whole.

As President Truman recently asserted, "Continuous research by our best scientists is the key to American leadership and true national security. This work may be made impossible by the creation of an atmosphere in which no man feels safe against the public airing of unfounded rumors, gossip, and vilification."

Challenge to Social Science

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THE INDUSTRIAL REVOLUTION is a term that the elder Toynbee used to describe the historical shift in the basis of human culture from agrarian to industrial. The student generally learns a few names of men associated with this period—Watt, Whitney, Hargreaves—and their respective inventions, but only rarely does he discern their relationship to the problems before which the world now trembles. The fact is, however, that the revolution is moving on more rapidly during his lifetime than ever before, and engineering, chemistry, electronics, aviation, biology, and many other sciences are contributing to it.

The intellectual equipment for making this change was perfected by the labors of a host of men, scattered over a period of two thousand years. The scientific method that they applied to the material world has loosed a torrent of discoveries.

Many results of these discoveries were beneficial and brought higher standards of living. Mass production could succeed only on a base of mass power to consume, more leisure, and the broadened knowledge and experience that stemmed from mass communication and transportation.

One profound change has been the shift from independence to interdependence. When the simple life prevailed, contacts were individual, relationships were uncomplicated and characterized by a high degree of self-sufficiency and independence. Today we know the paralysis that can occur with the breakdown of any of the numerous lines of supply within a nation.

Nations are as interdependent as their citizens. Vitally needed products must be exchanged throughout the world, and an economic depression in any leading nation means that all others will be similarly affected. Any science or organized knowledge is the joint product of men all over the world.

This interdependence has led to an extension of moral values from the personal and community level to the national and international level. Individual morality becomes inadequate when it is possible for a person to refrain from stealing from his neighbor, lying to him, cheating or killing him and yet advocate national or international policies that lead to mass destruction of peoples. The most humane and kindly individuals may be greatly disturbed at the suffering of one child but innocently contribute to wholesale suffering and death thousands of miles away.

Mass civilization has impersonalized relationships between men. When one killed with the sword, he saw his antagonist fall, saw his blood, and heard his dying gasps. To the killer this was real. In modern war a plane flies over a city, a man in the plane presses a button, and ten or ten thousand people may die. The killer himself is only the final link in a long, mechanized, and impersonal chain of events, and even he does not witness the deaths of the people he kills. Successful war now means total war, and the civilian comes to suffer more than the soldier.

Being moral involves, therefore, much greater knowledge of national and world events. It makes greater demands upon the intelligence of people who have become citizens of the world whether they happen to like it or not. Good intentions are less and less adequate to the situation.

Natural science has become "dehumanized," as James Harvey Robinson (7) so clearly described. Its adherents have in large measure become so specialized that they give little consideration to the effects of their discoveries on the population or how their techniques and knowledge might help solve problems. In this unawareness they have been burrowing into nature and throwing up great heaps of specialized information and expending little effort on organizing and utilizing it to best social advantage. As Robinson said a quarter century ago:

We are forced to ask ourselves whether it is safe, since our life has come to be so profoundly affected by a dependence on scientific knowledge to permit the great mass of mankind and their leaders and teachers to continue to operate on the basis of presuppositions and prejudices which owe their respectability and currency to their great age and uncritical character and which fail to correspond with real things and actual operations as they are coming to be understood. Even the more magnificent scientific discoveries, especially those of recent years, have not penetrated into our general education and are entirely disregarded in most discussions of social problems.

This has led to what a symposium of British scientists called "The Frustration of Science (2)." The original aims and basic intentions are clear enough. The physicist Harold Urey (8) says:

I believe I speak for the vast majority of all scientific men. Our object is not to make jobs and dividends. These are a means to an end, merely incidental. We wish to abolish drudgery, discomfort and want from the lives of men and bring them pleasure, comfort, leisure and beauty. Often we are thwarted but in the end we will succeed.

One sees on every hand, however, that Bacon's gunpowder, for example, can be used either for food or for homicide; Nobel's dynamite, as he discovered, for engineering or for bombs; the automobile and ship

for the spread of culture or for tanks and destroyers; the Wrights' airplane to bind the world more closely together or blow it to pieces; organic chemicals for life-saving drugs or incredibly potent poisons; knowledge of microorganisms for the conquest of disease or bacteriological warfare; and radioactivity for medicine and power or for the obliteration of cities and nations. How are we to determine what the alternative will be? We cannot follow our present rate of destruction very far and survive.

Men have begun to ask themselves, "What can we do to solve the frightening difficulties into which our distorted ingenuity has led us?" Since the rise of biology, psychology, sociology, and anthropology during the last century we have been compelled to recognize that it is possible to apply scientific procedures to the problem of comprehending, predicting, and intelligently controlling human behavior. The old stereotype of science as frozen content, limited to a small number of fields, persists, however, despite the fact that its history shows, in the words of Karl Pearson, that it "is not peculiar to a certain subject matter."

More specifically, a series of writers have maintained with increasing effectiveness that scientific methods are applicable to social problems—during the last century John Stuart Mill, Auguste Comte, and Karl Pearson; more recently Graham Wallas, James Harvey Robinson, Harry Elmer Barnes, and John Dewey. The last five years have brought the publication of Lundberg's *Can science save us?* (3); Williams' *Human frontier* (9), expressing the approach of the biochemist; *Human nature and enduring peace* (6), the psychological analysis of the war, edited by Gardner Murphy; and Stuart Chase's *Proper study of mankind* (1), giving the coordinated approach to many of many social scientists. We should not omit Lynd's admirable *Knowledge for what?* (4) and Mayo's *The social problems of an industrial civilization* (5).

Organizations, too, have been active—among them Yale University's Institute of Human Relations and the Society for the Psychological Study of Social Issues. Several foundations for humanities and scientific industrial relations are in process of development throughout the country. All these efforts point in the direction of a new synthesis of information from many fields, information which is relevant to the solution of modern problems.

The American sociologist Ogburn devised the term "cultural lag" to describe the failure of the social phase of culture to keep up with the physical. It is now a platitude to say that scientific methodology must be applied to human problems if we wish to reduce this ominous lag. What will this mean in the development and growth of the social sciences?

Social science is a flexible term, embracing history, economics, political science, and sometimes education, sociology, and psychology. Some institutions of higher learning are beginning to classify psychology with the biological sciences. Only in sociology and psychology have scientific methods been practiced systematically. If the social sciences are to grow—as they must if man is to survive—certain improvements are necessary.

(1) The success of the natural sciences can be credited very largely to the constant reconstruction of ideas. Proponents of the *status quo* are the villains of their history, when known at all. The experience of these sciences has been that there is no progress unless someone is continually finding fault with things. Only in this way can old concepts be strengthened and new ones discovered. Fending off criticism weakens a cause by denying it the opportunity to grow and to keep in close contact with a changing world.

It is not easy to invite criticism even in the physical sciences, where most data are inanimate objects. In the social sciences, where data are the intangible thoughts and emotions of people, this difficulty becomes the primary concern. What is its source?

In social inquiry we tend to identify our own ego with various concepts which we accept, and to regard criticism of ideas as destructive criticism of the personality holding them—as it too frequently is. It is tragic to see reputable social scientists falling victim to this tendency.

The solution has already been found, not only by physical science but by many ordinary people who have achieved the capacity to dissociate judgment of the man from the ideas held. There is need for social criticism if it is offered in a constructive spirit. Everyone should seek it eagerly and be able to profit from it, gaining the advantage of a great positive force. We agree that everyone is fallible. Science has shown how this fallibility may be combated most effectively in a way that preserves mutual respect and offers the thrilling experience that accompanies a joint search for truth.

(2) One of the primary objectives of criticism is stimulation of new ideas. Social science has heretofore looked too much to the past for answers to its problems. This does not mean that there is no value in the past. It does mean that the complex problems of an interdependent and technological universe are unique in human history and that unique solutions must be devised.

We venerate leaders of the past precisely because they were courageous and farsighted enough to challenge old concepts with new ones for a new age. The

fact that a problem exists is proof that old concepts have proven inadequate to the situation. The universe is dynamic and change is eternal. Human institutions and problems are the most rapidly evolving segments of it. Refusal to recognize and guide this change will merely insure greater confusion.

If history demonstrates anything it is that a frigid reception is invariably accorded new social proposals. The social sciences stand now in their development where the physical sciences stood in 1600 and its innovators may expect a similar fate. Will we again require 400 years to achieve our goal?

It is interesting to compare attitudes in the physical and the social sciences. We take pride in the newest and most modern gadget or technique. We are disturbed if the doctor evidences the slightest suggestion that he is “behind the times,” since this may mean needless suffering. But in social matters we are equally proud of beliefs which were current when diseases were treated by boring holes in the head. Barnes puts it picturesquely when he says, “The only place we prize antiques more than in our living rooms is under our hats.”

It is true, as many maintain, that we should show a healthy skepticism toward new propositions until they have been proven. It is interesting to note, however, that those who advocate such experimental testing of new concepts frequently do nothing to assist it and in fact may do a great deal to prevent it. We must devise ways to keep the intellectual concrete from setting too early and too hard.

(3) In the natural sciences we have learned the tremendous value of subsidizing the search for objective truth. This means criticism and new ideas against which there is determined opposition. Why?

Change in human institutions is thwarted by several forces. First is the immense power of custom; one discovers early in life that things are done according to a set pattern and that fundamental deviation from it will surely be accompanied by ridicule and social disfavor. Closely related is that intellectual inertia which manifests fear of anything new. This fear cannot be inborn, since the same people will show no such fear of new physical concepts or devices once they have become habituated to the idea of change. There is also a lack of the information necessary for enlightened action. Finally there is special interest in the *status quo*, which is a tremendous force.

How many agencies can the reader name that subsidize the analysis and reconstruction of human institutions without respect to the results? Yet the value of objectivity has been demonstrated in the physical sciences. Newton had no patents on gravitation, nor

did Pasteur and Koch have an investment to protect when the virus was discovered to be another cause of disease besides the bacterium.

The NAM will sponsor an investigation whose conclusion has already been established, and the CIO will spend money to prove the opposite. People in such organizations do not invite even the most helpful criticism. Lobbies, pressure groups, and influential business interests represent highly effective instruments for thwarting scientific attack on problems.

(4) Before any reliable information can be communicated we must be sure that our words symbolize something that really exists and furthermore that they convey the same conception to everyone who is influenced by them. This is the principal aim of semantics and propaganda analysis, which, together with logic and statistics, are the indispensable tools of the social scientist.

Although the original purpose of language was to communicate accurate information, its present misuse contributes to prejudices, destructive criticism, and frustration of new concepts. History uncritically preserves in its texts the most emotionalized and misleading language imaginable. Political economy and political science abound with sacred cows and verbal demons. Perhaps no language reform could succeed in making a true science of social problems but there is no doubt that decided improvement can be made.

In the natural sciences, use of Greek and Latin has provided a symbolism to avoid the changed meanings and affective connotations of popular usage. It is too much to expect that such a symbolism could be applied extensively to social problems. The reason is not far to seek. Those who support government by the majority must recognize that this majority is not likely to adopt such a mode of expression.

Fortunately, however, we do not have to resign ourselves to the nightmares of distorted meaning which the semanticists are able to select as examples of our everyday speech. The average person can grasp a few simple rules that will avoid the present confusion.

Let us illustrate one difficulty by returning to the word *criticism*. It denotes constructive analysis and yet hearing the word evokes a mental picture of an ill-adjusted, complaining egotist because these connotations have been built up through popular use. The semanticist would probably advise the use of another word, such as reconstruction. In a moment we will consider the operational approach to meaning.

(5) Social science tends to get lost in a forest of particulars. Facts, although they are indispensable, can never tell us anything by themselves. Conclusions must be drawn from them. Disciples of the monographic school of historians of a half-century ago

supposed that they could found a true science of history upon a massive accumulation of facts on the subject. But history as the record of human behavior can be understood and interpreted successfully only when there are some clearly defined standards for evaluation and objective techniques for processing data. Only in this way can the historian capture even partially the forces shaping events as they occur.

A few fundamental principles of human behavior are greatly needed for use in organizing its data. Institutions fail because they violate these principles—governments fall, parties go out of power, economic and social systems disintegrate. History lacks objective standards for evaluating its immense accounts. Facts are all things to all men and can be made to point in any direction.

Without a guide to their meaning, facts alone, however compendious, are almost useless. Historians select from a stockpile of past events (which make their own appear trivial) those showing what they wish to show. Thus we see the tremendous scholarship of Toynbee and Gibbon and of von Ranke and Robinson producing opposite theories, and the only basis for selection we have is our own prejudice and desire.

We have not yet realized the full significance of the elementary principle that there are causes for social phenomena. If we applied that principle we would renounce such attitudes as blame and condemnation of sin. These attitudes lead us away from an attack on causes and therefore away from cure and prevention of human ills. No physicist would kick his apparatus because it didn't work right.

What should we think of a medical science that concerned itself primarily with recording one-tenth degree fluctuations in the patient's fever, as economists chart their business cycles? What should we think of the physician who treated smallpox by covering up sores with flesh-colored cream? Yet this is what we are doing when we institute home relief.

Recognizing the principle of cause would mean also abandoning the prevalent attempt to interpret social phenomena in terms of what is "right" or what "ought to be." The scientific approach does not begin with ideas in mind about what nature "ought to do," but recognizes that fundamental laws operate to cause events to take place in the observed way. We are compelled to discover these basic realities and adjust our own acts accordingly so as to derive the maximum advantage and control of nature.

Science is pragmatic. Much scientific knowledge is based on what works, even when we lack exact information on how it works. But those who think they can get by with violating laws of human behavior denying basic human needs, because "it works," will

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soon find out that it does not work for long and that the cost of such short range pragmatism is very high.

(6) After investigation and criticism have disclosed tentative conclusions, expressed in accurate language—after the hypothesis has been established, what then?

What an idea really means to people, the true measure of its relative significance, can be discovered only by observing how their actions are affected. This truth has found many expressions from "by their fruits ye shall know them" in the Sermon on the Mount to the dictum of the physicist Bridgman that answers to questions can be realized only in terms of actual operations. If the difference between philosophy and science could be defined the distinction would probably have to be made on this action basis.

What we can get people to say and what we can get them to do are often very different things. Most legislators denounce lobbies and trusts. In view of their agreement their lack of action might at first be surprising. A federal judge recently spoke of the trust question as "a problem for Congress." But the yearly appropriation Congress makes for such prosecutions is less than what *one* corporation has spent on *one* antitrust suit. A bill on lobbies was recently introduced in the Senate but was stalled in subcommittee and has not even been able to reach the debating stage on the floor. There might be legitimate room for doubt about the most effective approach but there is no excuse for not undertaking some action that might produce results, even if several methods had to be tried.

The most frequent objection to the application of scientific methods to human problems is based on the belief that knowledge is certain and permanent in the natural sciences, whereas behavior difficulties are so complex that definite conclusions cannot be reached. People who hold this paralyzing belief do not realize first how much change is constantly occurring in the

principles of physical science and second, how successful we have already been in the analysis, prediction, and control of behavior. Our analysis is based upon the observed reality of fundamental motives which constantly direct our actions. Our real problem is to find what types of institutions can be most successful in terms of these realities.

The do-nothing attitude in respect to the social sciences often falls back on the "two sides to every question" stereotype. There may be any given number of hypotheses worthy of consideration when little evidence is available. As the evidence accumulates the number of tenable hypotheses decreases. It soon becomes clear which one is the most probable. We cannot avoid acting on some assumption. It is the constant purpose of science to make assumptions explicit and to relate them to facts as closely as possible.

Apathy about human affairs is tragic, because the reasons for it are perfectly apparent and remediable. Most people believe that modern problems are insoluble, at least for them. When they turn to social science they are crushed by the weight of details and bewildered by the indefiniteness and contradiction of authorities. The physical sciences, on the other hand, are forbidding because they are so technical and abstruse that the average man hasn't a chance. Fortunately, however, it is not necessary to understand the physics of the chain reaction in order to grasp the real social significance of atomic energy.

If the ordinary person had to become an expert in social technicalities to fulfill his duties as a citizen we might well forget all about having the majority exercise control over public affairs. But we do not all have to be experts if we get down to working agreement on some basic principles and encourage the critical ability to apply them. Only then can we look forward to a world made safe for human life.

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TECHNICAL PAPERS

Hemagglutinating Behavior of Mouse and Egg-adapted Type A (PR8) Influenza Virus¹

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Influenza virus undergoes a change when introduced into the mouse following either primary isolation or adaptation in the chick embryo (1, p. 357, and 3). Both Hirst (1, p. 357) and Wang (3) showed that the egg-adapted virus multiplies readily in the lungs of mice without producing either the clinical disease or histological changes. Death or pulmonary lesions will occur after the egg-adapted virus has had several passages through mice.

The present study indicates that mouse-adapted influenza virus undergoes a change when the virus is returned to the egg; although this change appears to be easier than the egg-to-mouse adaptation.

The PR8 strain of influenza virus A which was employed in these experiments has been maintained in the laboratory by allantoic passages through fertile eggs. Its virulence for mice had decreased so that the mean lethal dose which kills 50% of the animals (LD_{50}) per 0.05 ml intranasally was 10^{-2} . After 25 mouse passages, this mouse-adapted strain possessed an LD_{50} of 10^{-6} . These passages were performed by harvesting lungs 3-4 days following inoculation, making a 10% suspension in buffered saline by homogenizing in a Waring blender, and reinoculating into 3-4-week-old mice.

Ten-to-eleven-day-old embryos were inoculated into the allantoic sac with 0.2 ml of a 10^{-8} dilution of mouse-adapted or original egg virus. At 2-hr intervals, 5-10 eggs of each group were removed from the incubator and placed in the refrigerator. This was continued for every 2 hr up to 24 hr.

Allantoic fluid was harvested in the usual manner at each 2-hr period and titrated in the hemagglutination test by the pattern method of Salk (2) with human type O erythrocytes.

The data recorded in Fig. 1 are the results of a typical experiment with the 27th passage mouse strain. The egg virus was from a pool of allantoic fluid.

It was demonstrated that the egg strain produced hemagglutination at least 4 hr earlier than the mouse strain. Similar results were obtained with material from other mouse passages and other allantoic fluid pools. The earliest that hemagglutination was produced by the egg strain was 12 hr, while for the mouse strain it was 18 hr after inoculation. These were obtained in simultaneous titrations, using material from the 31st mouse passage;

¹ Aided by a grant from Hendricks Research Fund.

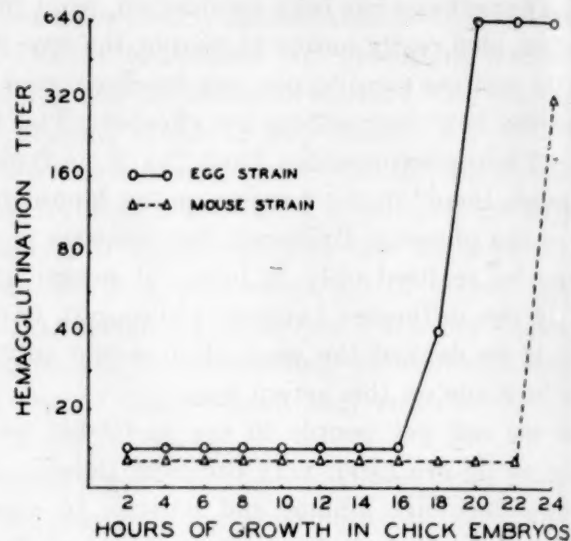


FIG. 1. Hemagglutinating ability (type O red blood cells) of mouse-adapted and original egg strain in the chick embryo. Type A (PR8) Influenza virus employed.

the egg material was from an allantoic pool not previously titrated. There was some variation in end points but when tested after 24 hr incubation, they were essentially the same for both strains. One egg passage sufficed to make the mouse strain indistinguishable from the original egg strain in hemagglutinating capacity.

When the mouse-adapted PR8 strain was cultivated in the mouse lung and hemagglutinating ability determined at 2-hr intervals, the results were essentially similar to those obtained by Wang (3). Perceptible hemagglutination with mouse lung virus was obtained within 6-8 hr after intranasal inoculation. As also observed by Wang, infection of chick embryos occurred more rapidly than hemagglutination.

The data reported here substantiate the observations of others (1, p. 357, and 3) that changes occur in the virus particle which is adapted to a different host. Whereas the results obtained by these workers indicate that there is a marked change in the virus when adapted to the mouse from the egg, little information is available concerning the reversal of this adaptative procedure. It appears, as Hirst suggests (1, p. 367), that adaptation to the egg is "a less drastic procedure than mouse adaptation."

Our data appear to agree with Hirst's findings that egg-adapted strains from a given epidemic do not differ significantly (1, p. 367). One may postulate, then, that the virus particle in adapting itself to a host alters itself to take advantage of the new host's metabolic systems. Thus, when the virus is introduced into a new host with a slightly different metabolic pattern, a probable rearrangement of the virus molecule occurs.

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Cytological Evidence Opposing the Theory of Brachymeiosis in the Ascomycetes

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Recently a collection of the discomycete, *Patella melanoloma*, was obtained by the writer from burnt-over ground in this area. The fungus has been maintained in culture, where it readily produces its fruiting structures or apothecia. The species is of particular interest because it is one of several discomycetes studied by Gwynne-Vaughan (1), the most outstanding contemporary proponent of the theory of double fertilization (two nuclear fusions) and brachymeiosis (two reductional divisions) in the ascomycetes.

Probably the majority of geneticists and most cytologists working on the ascomycetes have doubted for some time that these two processes occur. Thus far, however, no convincing evidence has been presented either to prove or to disprove the theory for those species in which these phenomena are said to exist. Most of the species of ascomycetes in which double fertilization and brachymeiosis have been reported to occur have proved unfavorable for genetical study. In those heterothallic species which might be used for genetical study such difficulties are experienced as inability to obtain a satisfactory percentage of ascospore germinations, or failure of the ascospores to occur in an orderly sequence in the ascus, or failure of the fungus to fruit well in culture. All the cytological evidence bearing on this subject has thus far been in the form of drawings and descriptions of sectioned material stained with the use of techniques which are frequently inadequate for revealing the chromosome numbers of the nuclei at various phases in the life cycle.

With the use of the propiono-carmin staining technique, recently employed with excellent results by Wheeler *et al.* (2) in a cytological study of ascus development in *Glomerella*, the writer has been able to observe the three successive nuclear divisions in the ascus of *Patella melanoloma* and to determine with certainty the number of chromosomes present during each division. One of the most important features of this technique is that it leaves the spindle fibers unstained and that the chromosomes stand out clearly in the nuclear vacuole. Photographs demonstrating the numbers of chromosomes in all three divisions in the ascus have been obtained and will be included in a paper to be published later.

Gwynne-Vaughan (1), in her study of this species, reported that the nuclei fused in pairs in the ascogonium to produce diploid nuclei. These diploid nuclei were believed to pair among themselves, migrate into the ascogenous hyphae, and finally fuse in pairs in the young asci. Thus each ascus was believed to contain a tetraploid nucleus. She stated that the tetraploid number of 8 chromosomes (4 pairs) was observed at metaphase of the first division in the ascus. These chromosomes were believed to pass in groups of 4* (the diploid number) to

opposite poles of the spindle. In this way the first reductional division was completed. Each daughter nucleus was then observed to divide mitotically, 4 chromosomes passing to opposite spindle poles. Then in the third division, each of the 4 nuclei was believed to undergo a second reductional division with 2 chromosomes (the haploid number) passing to opposite spindle poles. Therefore each of the 8 ascospores was supposed to receive a nucleus with only 2 chromosomes.

The writer is able to confirm Gwynne-Vaughan's report that there are 4 pairs of chromosomes present at the beginning of the first nuclear division in the ascus, and that a complement of 4 passes to each pole as the division is completed. In the second division also, 4 chromosomes appear and divide, a complement of 4 passing into each daughter nucleus. But the third division, instead of being reductional as Gwynne-Vaughan described it, is similar to the second division, and 4 chromosomes, rather than 2, pass into the daughter nuclei. The 8 ascospore nuclei, therefore, contain 4 chromosomes each. It is obvious from this brief description that the chromosome number is reduced only in the first division. The diploid number of chromosomes is 8 and the haploid number is 4. The third division is nonreductional. It is therefore obvious that brachymeiosis does not occur in this fungus. It is equally obvious that there can be no double fertilization in the life cycle.

The writer intends to extend these observations to other species in which double fertilization and brachymeiosis have been reported. The propiono-carmin technique is recommended as an efficient method for obtaining chromosome counts in the ascomycetes.

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Inability of Thymine and Adenine to Substitute for Pteroylglutamic Acid in the Folic Acid-deficient Rat

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Although it has long been recognized that thymine can replace folic acid for growth of microorganisms (8), it has not been emphasized sufficiently that both thymine and purine bases are required for this purpose (5, 6). If an analogous situation exists in animals, it might be expected that thymine alone would be ineffective in replacing folic acid in a synthetic type of diet which does not supply purine bases, and this has indeed been shown true for both the rat and the chick (1, 3, 4). Experi-

¹The authors are greatly indebted to Dr. E. E. Snell of the University of Wisconsin for his helpful suggestions and criticism. They also wish to thank Alice M. Bergdahl for assistance in obtaining the hematologic data.

ments wholly analogous to the bacterial growth tests, i.e., in which a dietary source of both thymine and purine bases has been supplied in an effort to duplicate the growth and hematopoietic effects of folic acid, have not been previously reported. We have therefore extended our previous work to include such experiments.

Sulfasuxidine (succinyl sulfathiazole). These data are pertinent in discerning the possible mode of action of pteroylglutamic acid in animal metabolism, since it has been postulated by Rogers and Shive (5) and Spies *et al.* (2, 7) that folic acid operates in the enzymatic synthesis of purines and pyrimidines.

TABLE 1

EXPERIMENT 1. EFFECT ON RATS OF THYMINE, ADENINE, AND ADENOSINE AS SUPPLEMENTS TO A PURIFIED DIET CONTAINING 2% SUCCINYL SULFATHIAZOLE (FOLIC ACID-DEFICIENT DIET)

Supplements	Initial weight in g of 28-day-old rats	Final weight in g of 63-day-old rats	Weight gain in g	R.B.C. (cells/mm ³ × 10 ⁻⁶)	Hemoglobin g/100 ml blood	Hematocrit (vol. %)	W.B.C. (cells/mm ³ × 10 ⁻³)	% Granulocytes	Total granulocytes (cells/mm ³ × 10 ⁻³)	Ratio of animals surviving
None	67	133	66	8.53	17.1	43.0	8.64	1.6	0.14	10/10
Thymine (150 mg/100 g)	66	141	75	7.91	17.9	41.3	7.02	1.7	0.12	10/10
Thymine (150 mg/100 g) + adenine sulfate (150 mg/100 g)	66	135	69	8.78	17.9	45.5	7.88	2.0	0.16	10/10
Thymine (150 mg/100 g) + adenosine (150 mg/100 g)	68	132	64	8.42	17.5	42.9	7.16	1.4	0.10	10/10
Folic acid (50 µg/100 g)	65	185	120	8.37	17.2	41.6	11.78	8.7	1.02	10/10

TABLE 2

EXPERIMENT 2. HEMATOPOIETIC EFFECT OF THYMONUCLEIC ACID ON FOLIC ACID-DEFICIENT RATS FED 2% SUCCINYL SULFATHIAZOLE

Supplement from 63rd day to 77th day	Weight in g at 63 days	Weight in g at 77 days	R. B. C.		Hemoglobin		W. B. C.		Granulocytes		Ratio of animals sur- viving
			$(\text{cells/mm}^3) \times 10^{-6}$		g/100 ml		$(\text{cells/mm}^3) \times 10^{-3}$		$(\text{cells/mm}^3) \times 10^{-3}$		77th day
			63rd day	77th day	63rd day	77th day	63rd day	77th day	63rd day	77th day	
2.1 µg folie acid	138	158	8.7	7.5	16.5	14.7	5.3	7.4	0.11	0.67	8/8
150 mg of thymonucleic acid \cong 15 mg of thymine	131	123	8.6	6.8	15.7	13.2	4.8	2.0	0.08	0.03	8/8
5 µg folic acid	140	179	8.7	7.5	16.4	15.2	5.6	9.7	0.12	1.43	10/10

Twenty-eight-day-old littermate rats and the basal diet containing 2% succinyl sulfathiazole as previously described (4) were used in each of the two experiments reported here. In experiment 1, using ten rats, the supplements were incorporated in the basal diet and fed ad lib. for a 5-week preventive period. In experiment 2 the supplements were fed daily for a 2-week curative period after a depletion of 5 weeks. The results are shown in Tables 1 and 2.

The data seem conclusive in demonstrating that neither thymine combined with adenine sulfate or adenosine, as in experiment 1, nor thymine and adenine supplied as thymus nucleic acid, as in experiment 2, show physiological activity in replacing folic acid for growth and hematopoiesis in the rat fed a purified diet containing

The possibility exists that folic acid may serve essential functions in the animal body other than hematopoiesis; and whereas thymine and adenine may replace folic acid for these, they do not do so for hematopoiesis, which is the limiting function in the experiments described here.

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Use of Silicones in Aerobiology

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In studies of organic and inorganic materials of the air, particularly in the epidemiology of rusts and other fungus diseases (4) and in allergy studies with pollen grains (1), it has been common practice to collect the specimens on glass slides covered with some adhesive such as vaseline, glycerine-jelly, or oil. In our investigations of airborne fungi and bacteria we have encountered temperatures as low as -48°C . At such low temperatures ordinary adhesives become too viscous or congeal and are unsatisfactory. The silicones made by the Dow Corning Corporation¹ seemed to offer possibilities as a substitute for the usual adhesives because of their retention of physical properties at low as well as high temperatures, and they were accordingly investigated. They have proved to be so satisfactory that it is considered worth while to call these new techniques to the attention of workers in this and related fields.

Slides coated with silicone grease (DC-4-ANC-128-A) have been used successfully in collecting rust, smut, and *Alternaria* spores from the air. Such preparations are superior to vaseline-coated slides for the following reasons: (1) The background is white, making an effective contrast. (2) The consistency remains unchanged at temperatures ranging from -75°C to over 200°C . (3) The slides can be sterilized, if desired, in dry heat for 2 hr at 180°C . Many other silicones are available which might also be used for this and similar purposes.

In ordinary studies of airborne fungi and bacteria, exposure of agar plates from airplanes has been common practice (3, 5). However, Proctor and Parker (1, p. 49) have shown that agar plates exposed to low temperatures will freeze and give sterile readings even in nonsterile air. This problem has been overcome by coating the bottom of a Petri plate with silicone grease, sterilizing at 180°C for 2 hr, exposing the plates from an airplane and pouring in melted agar on return to the laboratory. Under these conditions, bacteria and fungi produce satisfactory colonies. Fungi grow through the overlying agar to the surface and sporulate normally; bacteria and yeasts develop between the two layers, forming typical subsurface colonies. Some bacteria are freed when agar is poured in and colonies develop in or on the agar. Isolations from any of these colonies can be made without difficulty. The principal advantage of this method is that plates may be exposed to extremely low temperatures for an indefinite period without any physical change or danger of freezing. By this technique cultures have been obtained from plates which were exposed to air temperatures as low as -48°C .

It would appear to us that these two methods might prove very useful in many phases of aeromycology and aerobacteriology, particularly where exposures are to be

made at low or high temperatures. In routine exposures for stem and leaf rust studies, as well as for other cereal pathogens, silicones appear to be more satisfactory than vaseline. They should also be very satisfactory for the collection of pollen grains in allergy and other studies. For collecting microfauna and even small insects, the silicones would probably work equally well. They should prove of value also in fields other than aerobiology, particularly in snowflake and ice crystal investigation, and in studies of dust at high altitudes or even in the stratosphere.

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Relation of Surface Phagocytosis to the Fibrinous Character of Acute Bacterial Exudates¹

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Evidence has recently been presented that encapsulated bacteria which cause acute respiratory disease are phagocytosed in the body in the absence of opsonins by a mechanism termed "surface phagocytosis" (2, 8). Leucocytes operating in the presence of various tissue structures have been observed to ingest and destroy type I pneumococci, Friedlander's bacilli, group A hemolytic streptococci, and staphylococci (7). Although the encapsulated bacteria escape phagocytosis when floating freely in a fluid medium, they are readily phagocytosed when trapped against tissue structures by the leucocytes. Also, when caught in a sufficiently dense concentration of leucocytes, they may be pinned between the surfaces of two or more cells and thus phagocytosed (6). Of the microorganisms so far studied, only type III pneumococcus is resistant to surface phagocytosis (5). Its ability to escape the leucocytic pseudopods has been shown to be due to an outer "slime layer" of capsular polysaccharide which is present only when the organism is multiplying rapidly. When the slime layer is lost with aging of the bacterial population, type III pneumococcus becomes susceptible to surface phagocytosis.

Since leucocytes utilize tissue structures in phagocytosing encapsulated bacteria in the absence of antibody, it would seem likely that they may utilize in a similar manner the fibrinous strands that characteristically occur

¹ Aided by a grant from the Commonwealth Fund.

¹ Experimental material supplied by Dr. M. J. Hunter, Research Director, whose cooperation is gratefully acknowledged.

in acute bacterial exudates. To test this possibility, the following experiments were performed.

Type I pneumococci (A-5 strain) harvested from 4-hr broth cultures, were washed in gelatin-Locke's solution and centrifugalized (8). To the pneumococcal centrifugate were added rat leucocytes (2) which had been washed in the cold (4° C) in both gelatin-Locke's solution and citrated rat plasma² containing platelets from

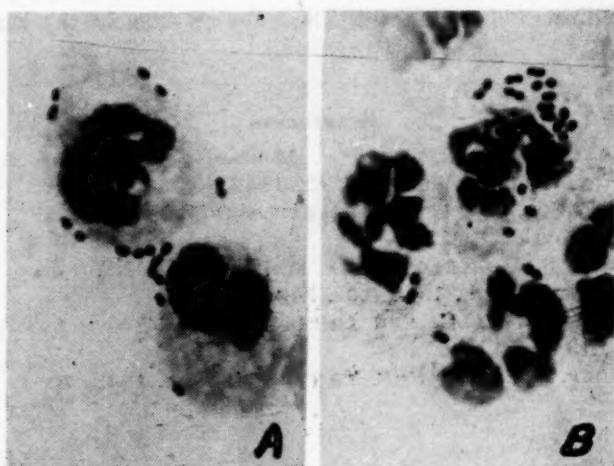


FIG. 1. A—Phagocytic test in unclotted plasma. B—Phagocytic test in clotted plasma.

the buffy coat. (The platelets were included to insure clot retraction when thrombin was added to the plasma.) The final leucocyte-pneumococcus suspension in plasma contained approximately 5–10 phagocytic cells and 25–30 pneumococci per oil immersion field. Phagocytic tests were carried out on glass cover slips coated with dry film³ to prevent spontaneous clotting of the plasma. When clotting was desired, one part of gelatin-Locke's solution containing 20 mg % of purified beef thrombin⁴ was added to five parts of the cell-plasma suspension. In all control preparations one part of gelatin-Locke's solution without thrombin was added. The cover slip preparations were covered with hollow ground slides, sealed with vaseline, and incubated for 1 hr at 37° C. Smears from the incubated preparations were stained with methylene blue. Clotted samples were fixed in Zenker-formol solution, sectioned, and stained by the Gram-Weigert technique.

As is seen in Fig. 1, phagocytosis failed to occur in unclotted plasma (A), whereas in clotted preparations (B) the phagocytosis was marked.

In order to observe the manner in which the leucocytes utilize the fibrinous strands in phagocytizing unopsonized pneumococci, pneumococcus-leucocyte mixtures in clotted plasma were studied in the warm stage of the microscope. Near the margins of the clot, phagocytosis was seen to result only when leucocytes succeeded in pinning the pneumococci against the fibrin strands. From this observation it was evident that the mechanism of surface phagocytosis in fibrin clots is essentially the same as that previously described in the lung (2, 7, 8).

² Rat plasma has been shown to contain no opsonins to the A-5 strain of pneumococcus I.

³ General Electric, Organosilicon Product, 9987.

⁴ Obtained through the courtesy of Dr. T. E. Weichselbaum.

Fibrin formation is a common feature of acute inflammation. Fibrinous exudates occur in acute bacterial infections of the lungs, pleura, peritoneum, meninges, and other tissues of the body. A significant portion of the fibrinous material in purulent exudates has recently been identified as desoxyribose nucleoprotein (1). Although beta hemolytic streptococcal exudates (group A) are relatively poor in both fibrin and desoxyribose nucleoprotein (3), most other bacterial exudates contain appreciable amounts of reticular substance. The present study demonstrates that strands of reticulum enable leucocytes to phagocyte encapsulated bacteria in the absence of antibody. Thus it may be concluded that the fibrinous properties of early bacterial exudates contribute to antibacterial defense by promoting surface phagocytosis. In chronic infections, on the other hand, where most of the leucocytes in the exudate are nonviable, the fibrinous strands may act as a mechanical barrier to recovery by interfering with adequate drainage of the lesions.

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A Method for Preventing Moisture Condensation During Photography of Tissue Cultures in Hanging Drops

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When tissue cultures grown in hanging drops over depression slides are taken from an incubator (37° C) and kept at room temperature, moisture condenses on the cover slip in the form of drops. These drops make it impossible to get clear photographs of the tissues. Various means have been devised to prevent condensation—the most common one is to keep the culture at incubator temperature. To accomplish this, some form of heating apparatus is placed on or near the stage of the microscope, but this may be a tedious process.

A simple procedure for preventing moisture from collecting on the cover slip has been devised. It consists of saturating the atmosphere around the culture with moisture and keeping the temperature fairly constant. Brass rings, such as those used by W. H. Lewis in his tissue culture work, are used. He found them useful for photomicrography, since they held the cultures at a uniform height above the slide.

These brass rings are 1 mm thick with a 25-mm outside diam and a 19–20 mm inside diam. About one-fourth of the ring is cut away, leaving it incomplete. The ring, held by forceps, is heated over a flame and then dropped into a dish of salvoline (6 parts vaseline and 1 part paraffin). It quickly sinks below the surface. It is then picked up, the excess salvoline is drained off and the ring, now completely covered with salvoline, is placed on an ordinary glass slide, well cleaned with 70% alcohol. When cool and hard, the salvoline holds the ring in place. The space enclosed by the ring is then filled with distilled water, most of which is at once drained off, leaving the surface of the slide within the ring covered with a thin film of water.

The cover glass containing the tissue culture is removed from its depression slide and placed on the brass ring. The salvoline holds it firmly in place. The layer of water inside the ring keeps the atmosphere around the culture saturated with water at a fairly constant temperature, so that water does not condense on the cover slip. If necessary, more water can be added to the space in the ring by means of a fine pipette placed at the opening in the ring. The tissue culture never comes in contact with the water. After photographing, the cover slip with its tissue culture is returned to its glass depression slide and the brass ring is ready for use again. Sometimes it may be necessary to add more salvoline to the top of the ring. This is easily done with a glass pipette filled with salvoline. The slide inside the ring must be completely free of salvoline. If it is not, then a freshly cleaned slide must be used; otherwise the distilled water will not form a thin even film over the glass slide. Glass rings or plastic rings can be used instead of brass rings.

Enzymatic Decomposition of Lignin¹

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Numerous claims have been made in the literature purporting to demonstrate the ability of microorganisms to utilize lignin as a sole carbon source, or purporting to demonstrate the existence of enzymes acting specifically on the lignin molecule. These reports are based on techniques which presuppose that lignin isolated by acid or alkaline treatment of plant material undergoes no important changes during its isolation (8, 9, 10, 13, 15) or that various color reactions can be used to detect the presence or disappearance of lignin (2, 6). Some work has been based on the assumed similarity in structure between lignin and tannic acid (1). Advances in our understanding of the chemistry of lignin indicate that these suppositions are very dubious (5, 12, 14). The

work of Brauns (3, 4) in isolating so-called "native lignin" by a process which minimizes structural alterations in the lignin molecule seemed to us to warrant an experimental reexamination of the ability of microorganisms to utilize isolated lignin and of the possible existence of lignin-oxidizing enzymes. Results of these studies to date are summarized here in a preliminary manner.

Lignin was prepared from 12-yr-old red sprucewood by the method of Brauns, and used in both nutritional and enzyme studies with fungi.

After a survey of a large number of species of wood-rotting fungi, good growth of several of these organisms was obtained after two weeks' incubation on media in which lignin was the limiting carbon source. This material will be reported in a separate communication (7).

Studies on a lignin-oxidizing enzyme were carried out, using the absorption of oxygen measured in a Warburg manometric apparatus as an indication of enzyme activity. A reliable source of enzyme was found to be commercial mushroom spawn,² which is an intimate mixture of mycelium of *Agaricus campestris* and well-decomposed horse manure. Conditions used in the preparation of this material are such that it is essentially a pure culture of this organism. A dry, stable preparation of the enzyme has been obtained by the following procedure:

Mushroom spawn is mixed with three times its weight of distilled water in a Waring Blender for 3 min. The resulting mash is subjected to a pressure of 15,000 psi in a Carver press and the press juice is dialyzed for 48 hr in Visking cellulose sausage casing against cold running tap water. The dialyzed solution is removed from the casing, cooled to 5° C, and to it is added two volumes of cold acetone. The resulting precipitated solution is cooled to 5° C, and the brown precipitate is centrifuged down and washed twice with cold 66% acetone. The precipitate is finally dried at 35° C under aspirator pressure. One lb of spawn yields 2–3 g of this dry preparation. The concentration of solids is reduced from 20 mg/ml in the original press juice to 6 mg/ml in the dialyzed solution, and to 2 mg in the acetone precipitate.

The enzyme is activated by citrate and phosphate ions and it is therefore buffered to pH 6.0 with McIlvaine's buffer (11) for activity measurements. Under these conditions 75 cu mm of oxygen are absorbed in the first hour when 1 ml of an aqueous solution containing 3 mg of enzyme is incubated with 1 ml of an aqueous lignin suspension containing 30 mg lignin/ml. The enzyme is quite stable in acid solution (pH 4.0–6.5), but loses activity rapidly at pH values higher than 7. The pH optimum for enzyme activity is 5.7–6.0, with a temperature optimum close to 40° C. Under optimum conditions, the activity of a solution of enzyme is proportional to its concentration.

It is believed that this enzyme is not identical with any of the known phenol oxidases, since mushroom sporo-

¹This work was done under Contract No. N7 onr 397-4 between the University of Maryland and the Office of Naval Research. The project was initiated at the suggestion of the Prevention of Deterioration Center, National Research Council.

²The mushroom spawn used in these experiments was obtained from the L. F. Lambert Company, Coatesville, Pennsylvania.

phores (a recognized source of tyrosinase) do not yield a product having activity. The enzyme is not activated by copper ions and is completely inactivated at pH values higher than 7. A study of the action of various enzyme inhibitors supports the nonidentity of this enzyme with any of the known copper-containing enzymes.

Studies are now in progress on the effect of this enzymatic reaction on the structure of the lignin molecule and on further purification of the enzyme. A detailed account of the work summarized here will be published in another journal.

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The Hemostatic Activity of Amniotic Fluid¹

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During studies of the coagulation mechanism in pregnancy it seemed of interest to investigate the action of amniotic fluid. This fluid was collected in a sterile syringe by aspirating the intact membranes of women in labor. The Lee and White clotting test was done, using four 12×75-mm glass tubes. One-tenth cc of amniotic fluid was added to each of two tubes and an equal amount of saline to each of two control tubes. Freshly drawn venous blood was added in 2-cc amounts to all four tubes, which were then incubated at 37° C. The end point taken was that at which both tubes of each set could be inverted completely without spilling. Results are shown in Table 1.

It can be seen that one part amniotic fluid, when added to twenty parts of blood, can cut in half the time required for clotting.

It appeared that by studying the behavior of amniotic fluid with oxalated plasma and fibrinogen solution² we

¹Supported in part by grants from the Blood Grouping Laboratory, Children's Hospital, Boston, Massachusetts, and the Charles H. Hood Foundation, Boston, Massachusetts.

²Supplied by courtesy of Dr. John Edsall, Department of Physical Chemistry, Harvard Medical School, Boston.

might be able to identify its place in the coagulation mechanism. The effect of amniotic fluid on the rapidity

TABLE 1
CLOTTING TIME

Specimen	Number of tests	Controls	With amniotic fluid
		Min	Min
A1-19	5	7.0	3.5
A1-21	3	7.5	3.0
A1-20K	4	7.8	3.4
A1-19W	3	7.7	3.4
A1-25S	6	7.5	6.0
A1-27	3	5.8	4.2
A1-28	7	6.3	3.6
A1-30G	15	8.0	3.6
A1-31	4	8.7	2.8
A2- 4	7	10.0	3.9
A2- 4S	3	8.0	2.6
A2- 5A	8	9.0	4.0
A2- 5N	5	9.3	2.7
A2- 5S	5	9.6	3.4
A2- 9W	5	7.5	3.6
A2-15A	4	8.3	3.5
A2-24	4	7.7	3.1
A2-25B	8	10.0	3.7
A2-24N	3	7.5	3.1
A3- 1G	5	8.7	2.4
A3- 2W	5	9.2	3.9

TABLE 2
RECALCIFICATION TIME

Specimen	Controls*	Plus 0.1 cc amniotic fluid†
	Sec	Sec
A1-19	76	46
A1-21	85	55
A1-20K	100	60
A1-19W	85	25
A1-25S	142	71
A1-27	131	55
A1-28	177	52
A1-30G	145	42
A1-31	111	47
A2- 4	140	56
A2- 4S	125	49
A2- 5A	93	53
A2- 5N	97	37
A2- 5S	110	61
A2- 9W	93	56
A2-15A	115	59
A2-24	135	65
A2-25B	145	73
A2-24N	145	63
A3- 1G	137	61
A3- 2W	120	36

* Recalcification time for 0.1 cc of 0.025 *m* calcium chloride, plus 0.1 cc physiologic saline, and 0.1 cc fresh plasma (0.5 cc of 0.1 *m* sodium oxalate to 4.5 cc blood).

† Substituting 0.1 cc fresh amniotic fluid for saline in recalcification.

of clot formation in recalcified plasma is illustrated in Table 2. These data indicate that amniotic fluid decreases the clotting time of recalcified oxalated plasma.

Preliminary experiments showed that amniotic fluid alone would not clot oxalated plasma; therefore it does not act like thrombin or trypsin, which clot oxalated plasma without added calcium. Amniotic fluid contains no prothrombin, since a clot will not form in prothrombin-free, oxalated plasma on the addition of calcium, thromboplastin, and amniotic fluid. Amniotic fluid does not decrease the plasma prothrombin time in the one-stage method.

TABLE 3
CLOTTING TIME

Specimen	Hemophilic blood	With 0.1 cc amniotic fluid
	min.	min.
A2-24	54	4
A2-25B	54	3.8
A3- 1G	54	3.5
A3- 2W	54	3.9

Amniotic fluid has a marked antihemophilic action *in vitro*. Table 3 shows the effect of .1 cc of amniotic fluid on the clotting time of a hemophiliac who was resistant

to therapy with Fraction 1 and fresh frozen plasma. It can be seen that the amniotic fluids produced clotting times with hemophilic blood comparable to those they gave with normal blood, whereas the hemophilic control tubes clotted in 54 min.

It would appear that amniotic fluid acts like thromboplastin in its effect on oxalated plasma. This activity is preserved for several days by storage in the deep freeze at -10°C but deteriorates within 1-3 days on standing at room temperature or in the ice box. The activity is nondialyzable. Boiling strongly for 5 min destroys it, although it is stable at 60°C for 30 min. Furthermore, it is entirely inactivated by small amounts of heparin. Various incubation tests which were done with amniotic fluid and fibrinogen clot or plasma clot showed no evidence of fibrinolytic power in amniotic fluid. Clotting tests of amniotic fluid with fibrinogen solution verify the lack of thrombic or prothrombic activity.

Uncontaminated amniotic fluid collected during labor contains a coagulant. This coagulant is thromboplastic in its behavior and antihemophilic. It is possible that amniotic fluid initiates clotting of shed intra-uterine blood and therefore plays an important part in normal postpartum hemostasis.

Comments and Communications

The AEC Loyalty Oath

A letter that I wrote some time ago to Dr. Detlev W. Bronk, chairman of the National Research Council, in connection with the loyalty oaths now required of Atomic Energy Commission Fellows, is still timely. One of the points made in this letter is, indeed, strongly emphasized by the recent proposal, embodied in the O'Mahoney Amendment to the Independent Offices Appropriation Bill, for a mandatory FBI investigation of all AEC fellows: namely, the point that it is difficult to contain measures of this kind within those bounds which might be suggested by prudence or by a decent instinct of self-restraint.

Basically, the issue here is one of political freedom. The denial of educational rights or privileges to a citizen who would be eligible for them were it not for his failure to measure up to some arbitrary political test is a clear violation of the principles upon which our republic was founded. The essence of the matter has been stated with complete clarity by Mr. Justice Stone in his celebrated dissenting opinion (later adopted by a unanimous court in a spectacular reversal of its decision) in the so-called "Flag Salute Case"—*Minersville School District et al., vs. Gobitis*, 310 US 601. That opinion should be read by anyone interested in the present discussion. Any attempt to distinguish between the situation met in the "Flag Salute Case" and the present one will only bring out the fact that the distinctions are completely secondary.

My letter follows:

Dear Dr. Bronk:

The statement issued by the Atomic Energy Commission on May 22 concerning the oaths and affidavits which will henceforth be required of holders of A. E. C. Fellowships is now available in its entirety, as published on page 552 of "Science" for May 27, 1949. Previous fragmentary reports concerning this statement had caused me to weigh its possible implications with great care. As a member of one of the boards created by the Council to pass on applicants for the A. E. C. Fellowships, I felt I should formulate and make explicit my own attitude toward the new situation. With the publication of the full statement before me, I am now able to arrive at a definite conclusion. I am therefore writing you to request that my resignation from the Postdoctoral A. E. C. Fellowship Board for Mathematics, Physics, and Chemistry, already placed in your hands under date of May 10 for reasons of a purely practical nature, be made effective at once.

A full statement of my reasons for this request would doubtless be inordinately long. There are, however, three main points which I might make here by way of briefly explaining those reasons. Fundamentally, it seems to me, the imposition of political conditions upon the pursuit of scholarship, however supported, is contrary to the political principles on which our nation is founded; prejudicial to the proper development of basic research in the United States; and most difficult to contain within those limits which the proponents of the current measures appear to accept as necessary. If I were not opposed to these measures on grounds of principle, I would nevertheless wish to withdraw from the atmosphere of suspicion which they will inevitably generate unless they are modified in the sequel by a practice of confining loyalty investigations of fellowship holders to those cases where classi-

fied research is involved. Finally, even if the submission of sworn statements were to be reduced in this manner to a kind of empty ritual, it would nevertheless be a ritual in which a young man, already idealistically dedicated in his own eyes to the service of his countrymen, would participate only with a certain sense of humiliation and a corresponding feeling of resentment; and I could not bring myself to continue a remote but identifiable association with the compulsion to participate. On this last point I recall with clarity the feelings I experienced when required to take the so-called Teacher's Oath some years ago in Massachusetts, an oath which I could and did take with a perfectly clear conscience and without reservations.

You will understand, I am sure, that this letter, being an expression of conscientious beliefs and not a discussion of mere practical arrangements, is a communication which I do not feel bound to hold private.

MARSHALL H. STONE

The University of Chicago

Method for Supplying a Laboratory with Warm Sea Water in Winter

One of the handicaps faced by the biologist working in northern waters is the long winter period when the water temperature is too low for active functioning of many invertebrates. In our case this period, when the water temperature in Long Island Sound is 5.0°C or less, may extend from four to almost five months. In severe winters a temperature of -1.5°C is often recorded (LOOSANOFF, V. L., *Ecology*, 1937, 18, 506). Under such conditions many forms are hibernating, while others are less active than at higher temperatures.

During the last five years we tried to overcome this difficulty by artificially increasing the temperature of sea water used in our experiments. The first attempts, which consisted in maintaining a high temperature in the experimental aquaria by means of electric heaters, were rather promising because they showed that oysters kept under such conditions could be induced to develop ripe eggs and spermatozoa even in the middle of winter (LOOSANOFF, V. L., *Science*, 1945, 102, 124). However, since the use of electric heaters was rather expensive, and because there were certain objections to keeping metal heaters and experimental animals in the same water, we did not consider the method entirely satisfactory and continued to seek a better one.

The principle of our present method is rather simple. Cold sea water is passed through a coiled lead pipe, which is immersed in a large tank filled with warm fresh water. The temperature of this water is maintained at the desired level by a gas flame regulated by a pilot light thermostat (Fig. 1, A). The temperature of sea water in the lead pipe leaving the tank is regulated by an electric thermostat, the bulb of which is attached to the pipe itself. This thermostat is also connected to the magnetic gas valve (Fig. 1, B) of the gas burner. If the temperature of outgoing warm sea water in the lead pipe decreases below a certain minimum, the thermostat sends a signal to the magnetic gas valve, which increases the gas flame. To prevent the stratification of warmer water in the upper part of the tank, a strong stream of air bubbles is continuously passed through the tank. In gen-

eral, the system is simple and can be installed by a person familiar with installation of domestic hot water heaters. Ours was installed by our laboratory mechanic, Joseph Lucash.

The advantages of having warm running sea water in a laboratory are numerous, the most obvious being the possibility of conducting throughout or almost throughout the year many experiments which formerly had to be

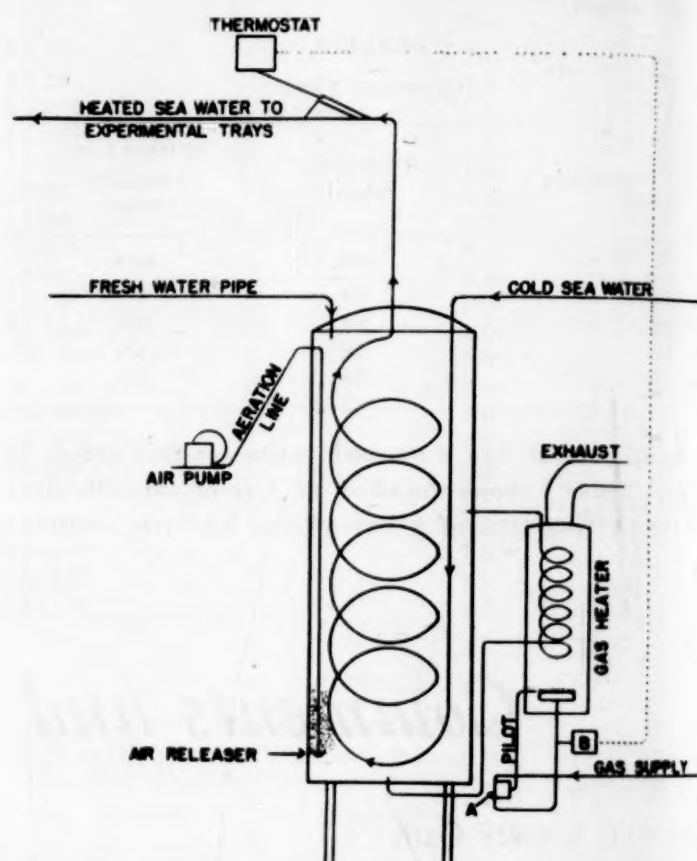


FIG. 1. Diagram showing method of raising temperature of cold sea water.

confined to the relatively short summer period. For example, by subjecting adult clams, *Venus mercenaria*, to gradually increasing temperatures during January, we induced them to spawn in February and March and grew their larvae to metamorphosis. For several years oysters were conditioned in the same way, and recently my colleague, Harry C. Davis, was successful in obtaining heavy sets of oysters in the middle of winter. No doubt similar success can be achieved with other forms which normally are inactive in winter.

By keeping the animals during the cold period at desired temperatures, laboratories can be assured of a sufficient supply of biological material, which is ordinarily unavailable in winter. For instance, we already know on the basis of our experience that embryological studies on eggs of some lamellibranchs can now be continued on almost a year-round basis. Thus, at least in this respect, we can hope to accomplish as much in one year now as could be done formerly in three or four.

Another advantage of a continuous supply of warm sea water in winter is that it is so easy to maintain streams of different temperatures by mixing warm and cold water in different proportions. We use streams of about 5.0 , 10.0 , 15.0 , 20.0 , 25.0 , 30.0 , and even 35.0°C .

Water of such temperatures, or any other temperatures within this range, can be prepared by having constant level jars of cold and warm water and by regulating the flow from these jars into a mixing chamber where the desired temperature is attained. From the mixing chamber the water will flow into the trays or aquaria containing the experimental animals. Because the temperature of our cold water is very uniform, adjustments are seldom necessary to compensate for fluctuations.

Having running water of different temperatures offers an opportunity to experiment simultaneously with groups of organisms kept at such temperatures. For example, we used our facilities for observations on growth of adult oysters at temperatures of 10.0, 15.0, 20.0, 25.0, and 30.0° C; on development of eggs and growth of larvae of different mollusks; in studies of some phases of physiology of oysters and clams, such as gonad development and spawning; and in many other experiments.

VICTOR L. LOOSANOFF

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Toxicity and the Chemical Properties of Ions¹

The mechanism of the toxic action of drugs has long been a controversial subject. Attempts at an elucidation of the problem include correlations between toxicity and molecular properties. The older physiologists and medical men are, in the main, opposed to any such correlation; the younger biochemists are for it. The more conservative investigators have much negative evidence to support their view, for usually when a drug is administered no one has the slightest idea what happens thereafter, other than the end result. Those who believe in an association between the physiological effect and molecular pattern of a poison have little evidence but much confidence to support their view—a view which they regard as the intelligent one, for, to what else can toxicity be due?

A study of the poisonous action of inorganic salts on slime molds should simplify matters, for the ion of a metal has a far less intricate structure than, for example, a molecule of cocaine, and a primitive form of life is devoid of the complexities of higher organisms.

The slime molds are Myxomycetes to the botanists, who regard them as plants, and Mycetozoa to the zoologists, who think these molds are animals. To medical men, slime molds are just protoplasm, far removed from the intricacies of the human body and therefore having little bearing on medical physiology. But perhaps the difference between the protoplasm of lowly organisms

and that of higher forms of life is not always as great as imagined. Lacking the differentiations which tissues present, the protoplasm of a slime mold reveals correlations which are obscured in highly complex organisms. Furthermore, the visible effect of a toxic agent on a slime mold may be directly observed through the microscope.

The degree of toxicity of a poison acting on a slime mold is determined by a number of pathological changes which occur in the protoplasm; among them are the periods of time necessary to kill, to stop protoplasmic flow, and to produce injury. The degree and kind of injury are also significant criteria; among these are gelation, solation, syneresis, blistering, surface rupture, and general disorganization.

Results of studies on the poisonous actions of anesthetic agents, drugs, and metallic salts on protoplasm were reported at an Army Symposium in June 1948.² The discussion there, and later elsewhere, led to numerous comments and criticisms, both adverse and constructive. They are repeated here in the belief that they will prove of interest not only to toxicologists, biologists, and medical research workers, but to chemists as well, for they deal as much with the physical chemistry of solution as with toxicity.

I had found a correlation between the anesthetic effects of CO₂ and N₂O and their isosteric properties (*Science*, 1948, 107, 15). The correlation was questioned because, so it was said, the protoplasm is not in contact with the gas, CO₂, but with carbonic acid. This is an old problem, and has long since been answered by both biologists and chemists. Of the several kinds of molecules and ions which CO₂ in water may present, it can be experimentally shown, by a process of elimination, that only the CO₂ molecule is responsible for anesthetic and other toxic effects. There are several ingenious experiments in physiology which demonstrate, by taste and color indicators, that an acid condition is established within living tissue when an alkaline solution is added outside, due to the rapid entrance of CO₂ as such. Few substances enter a cell as freely and as rapidly as does carbon dioxide, and it enters primarily as the CO₂ molecule.

The evidence from the physical-chemical side is of the same sort. H. B. Bull (*Physical biochemistry*, New York City: John Wiley, 1943) states that "at equilibrium, the amount of dissolved CO₂ is about 1000 times the amount of hydrated CO₂, i.e., of carbonic acid." This means that instead of having no free CO₂, there is some 99 percent of it when CO₂ is dissolved in water. The correlation between the isosteric and the anesthetic properties of the gas must, therefore, fall, if it is to fall, on other grounds.

A further criticism, directed against physical-chemical interpretations of the toxicity of metallic salts, involved the validity of the assumption that the metal ions are present as free ions. That hydrates and complexes are formed in solution is, of course, well known. Salts such as those of Al and Zn are particularly bothersome from

² Army Chemical Center, Edgewood Arsenal, Maryland.

¹ A number of chemists have contributed to these comments, some of them unknown to me, speaking in group discussions. Rather than attempt to select those whose comments should be acknowledged, I shall express my indebtedness to all collectively, and disclaim for myself any credit for the more fertile suggestions. I need only add that the physiological work on the toxicity of salts reported here was done in my laboratory by myself and my assistant, whose presence I owe to the Sloan-Kettering Institute for Cancer Research.

this point of view and are therefore frequently omitted from toxicity series. They not only hydrolyze readily, forming weak bases, but produce soluble complexes, leading to such ions as $[\text{Al}(\text{H}_2\text{O})_4(\text{OH})_2]^+$.

The case of mercury is a special one. HgCl_2 is but slightly dissociated in solution, and the concentration of Hg^{++} is correspondingly low. But mercury salts of oxygen acids are capable of giving high Hg^{++} concentrations. Mercury poisoning by $\text{Hg}(\text{NO}_3)_2$ is therefore due to free mercury ions.

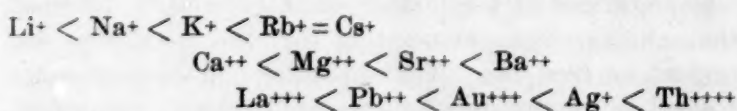
AgNO_3 , which I had regarded as a clear case of simple dissociation, was said to be another "troublemaker," an appellation which I had given to ZnCl_2 and AlCl_3 . But this does not appear to be true of AgNO_3 . The extent of hydrolysis of any given salt in aqueous solution can be calculated from the strength of the base, the metal hydroxide, and the acid. In the case of AgNO_3 , hydrolysis and complex formation, if any, are negligible, and the solution can be considered as one of Ag^+ and NO_3^- ions.

As for ZnCl_2 , it, too, in dilute solution, consists largely of the simple ions Zn^{++} and Cl^- . Hydrolysis, however, is great.

Accepting, therefore, as we apparently must, the fact that certain metals assumed to be responsible for the toxic effects of their salts are actually present as free ions in solution, we may seek in the physical and chemical properties of these ions an explanation of their toxicity.

A toxicity series such as $\text{Na}^+ < \text{Ba}^{++} < \text{Au}^{+++} < \text{Th}^{++++}$ is readily explained in terms of valence and charge. That such an analysis has some meaning is seen in the relative capacity of these ions to precipitate colloidal suspensions. But there are striking exceptions to a valence interpretation of toxicity. Monovalent Ag^+ is highly toxic, far more so than divalent Ca^{++} and trivalent La^{+++} . Very significant also is the fact that within any one valence group there are pronounced differences in toxicity. Thus, among the divalent cations, Ba is far more toxic than Ca.

Ionic series are frequent in chemistry and biology. The seriation is based on various reactions, on protein coagulation, sensory responses (FRINGS, H., *J. Comp. physiol. Psychol.*, 1948, 41, 25) cell permeability, adsorption, zeta potentials, and colloidal precipitation (FREUNDLICH, H., *Kapillarchemie*, Leipzig; Akademische Verlagsgesellschaft, 1934). Usually these lyotropic salt series are presented in one continuous line, but this is not always feasible, for there is frequently much overlapping; furthermore, the less toxic mono- and divalent ions often constitute a clear-cut series of increasing toxicity, whereas the more poisonous metals form a heterogeneous group. I prefer several distinct series, and I prefer, too, a staggered arrangement, as it better illustrates the experimental facts. For the protoplasm of slime molds, the complete toxicity grouping:



The hydrogen ion, itself highly toxic, is not involved in the toxicity of the salt solutions here mentioned. The pH

of all solutions used was near neutrality, and slime mold protoplasm thrives well at any pH above 4 and below 8.

Molecular interpretations of lyotropic series have been numerous. Valence and atomic weight are the first obvious correlations to be made with toxic effects. From top to bottom and left to right in the periodic table is the general rule for the increasing toxicity of the elements.

The unexpected position of certain ions in the third of the foregoing groups is more difficult of interpretation, but there are a number of atomic properties which appear to bear on the anomaly. The position of the ion in the electromotive force series correlates with toxicity to some extent. Five highly toxic elements, Cu, Ag, Hg, Pb, and Au are grouped together in the emf series. Of possible significance is the second electronic ring, that adjoining the outer valence orbit. Thus, Ag, Pb, and Au are all highly toxic and all have 18 electrons in the second orbit. The meaning of such a correlation would lie in its influence on the activity of the ions, on their tendency to form bonds with atoms which are part of the protoplasmic structure. Resonance is another property of molecules which has come into the biological picture of late. L. Pauling (*The nature of the chemical bond*, Ithaca, N. Y., Cornell Univ. Press, 1945) calls attention to resonance as a likely factor in physiological activities, to which W. T. Astbury (chapter in *The structure of protoplasm*, Ed. by William Seifriz, Ames, Iowa: State College Press, 1942) adds, "It may well be that resonance and the hydrogen bond are of more importance to physiology than any other two facts in chemistry."

It is upon still another property of ions that I wish to lay particular emphasis. There is a very close correlation between the toxic action of ions and their hydration. Protoplasm is largely water and lives in an aqueous medium. Hydration must, therefore, play a major role in physiological reactions. The order of hydration of the monovalent ions is: $\text{Li}^+ > \text{Na}^+ > \text{K}^+ > \text{Rb}^+ = \text{Cs}^+$; for the divalent metals it is: $\text{Ca}^{++} > \text{Mg}^{++} > \text{Sr}^{++} > \text{Ba}^{++}$. These are both the order of increasing toxicity. Relative hydration, therefore, correlates perfectly with degree of toxicity.

Some questions have arisen over types of hydration, over arrangement and density of the hydration layer. I therefore quote J. D. Bernal and R. H. Fowler (*J. chem. Phys.*, 1933, 1, 515) who state simply that Cs^+ is not hydrated and Li^+ is highly hydrated.

Water is an associated molecule, tetrahedral in structure. Bernal and Fowler compute ionic hydration from the maximum packing of the tetrahedrons, and find the order of hydration of the monovalent cations to be as given above, which agrees with results from all other sources (HARNED, H. S. and OWEN, B. B. *The physical chemistry of electrolytic solutions*, New York City: Reinhold, 1943.)

Harned and Owen point out that the ionic field is $\frac{1}{r^2}$, and hydration is, therefore, in inverse ratio to the ionic radius. The radius of the Li^+ ion is small enough to attract water molecules, whereas the large Cs^+ ion does

not permit the ion to hold a water layer. Thus do ionic radii, fields, hydration, and toxic effects run parallel to each other.

The role of hydration is a shielding one. It determines whether or not a toxic ion can exert its effect, but it does not determine the innate toxicity of the ion; i.e., if an ion is in itself not toxic, the absence of a protective water layer cannot make it so. A hydrated layer can protect but it cannot activate. Mobility is a measure of the activity of the ion and therefore must determine, in part, the nature of the reaction between ion and protoplasm.

The order of mobilities of five monovalent ions is (BRIGGS, D. R. *J. phys. Chem.*, 1928, 32, 1646):

Li	Na	K	Cs	H
33.4	43.5	64.6	68.0	315.0

and this is the toxicity order. But mobility is itself dependent upon hydration. The order of ionic mobility parallels that of hydration and therefore of the toxicity of the mono- and divalent ions. Cs^+ is about twice as mobile as Li^+ . Li^+ , as $\text{Li}^+ \cdot n\text{H}_2\text{O}$, becomes then the ion with the smallest radius, greatest field, maximum hydration, minimum mobility, and least toxic ion in the series. Cs and Rb, with numerous electron shells and therefore large radii, have weak fields, low hydration, and high mobility. They are, consequently, more toxic, being more active and having more direct contact with the protoplasm. The difference in the fields of Cs and Rb is slight; one would, therefore, expect that there would be slight difference in their toxic effects, and this proves to be true—it is difficult to distinguish the poisonous action of the two.

The third group of ions listed above is a heterogeneous one. The highly toxic Th^{4+} ion is of large size, heavy weight, great charge, and low hydration; Au^{3+} is the same; Pb^{2+} also, but to a lesser degree. Their toxicity therefore correlates with their physical qualities. The toxicity of La^{3+} , however, is surprisingly low for a trivalent metal, being less than Ba^{2+} . Trivalent Au^{3+} , on the other hand, is highly toxic. Hydration helps in part to set the matter straight. If we compare Ba^{2+} , La^{3+} , and Au^{3+} , we find that Ba^{2+} is highly toxic for a bivalent metal; its charge is not excessive but its hydration is low. La^{3+} is a heavy metal ion of large size and great charge; it should therefore be quite toxic, but it is much more heavily hydrated than Ba^{2+} ; the protoplasm is consequently protected against it. Au^{3+} has all the properties of La^{3+} except its hydration; it should therefore be highly poisonous, and this it is.

Ag^+ , because of its position in the third group with other exceedingly toxic elements, presents a special case. It is a large ion, and not highly hydrated, but these two facts alone are not enough to establish its high toxicity. The reaction between protoplasm and an ion is determined by the thermodynamic properties of the ion and by the selectivity of protoplasm. The former include the several properties so far presented, but they are not equally effective. Mobility and hydration dominate among the lighter elements. These two properties be-

come increasingly less significant with increase in atomic weight. Among the heavier metals, mobility and hydration play a lesser part.

Electronegativity, indicated by position in the emf series, determines the force with which a metal attracts electrons and therefore the ease with which it forms combinations with other substances. In the present case, these other substances are the protein constituents of protoplasm. Thus may we say that ionic mobility is a primary factor in determining toxicity among the lighter metals, whereas electronegativity is primarily the factor in determining the toxicity of the heavy metals. The long-recognized correlation between toxicity and atomic weight is here realized. Mobility decreases with atomic weight, but electronegativity increases, being greatest in the noble metals, among which Th, Ag, Au, Hg, etc., are the most poisonous of elements.

My interest in those physical properties of metals and organic compounds which explain their toxicity has centered primarily in the hydration and mobility of ions and in the structural patterns of molecules; but the further one looks into other properties the more nearly perfect the parallelism becomes. This is seen in the isosteric properties of CO_2 and N_2O (LANGMUIR, I., *J. Amer. chem. Soc.*, 1919, 41, 1543). It is also obvious in a number of other properties of those elements considered here. The coagulating power of ions is of the same order as their ionic mobilities (PAPPADÀ, N. *Kolloid Z.*, 1909, 14, 56). Furthermore, an ion which moves into an interface readily, because of high mobility, will for the same reason lower the potential and the surface energy.

Adsorption, likewise, nicely parallels both the physical and the physiological properties of ions. G. W. Searth (*General physiology*, New York City: John Wiley, 1930) points this out in listing the order of adsorbability, which for the monovalent and divalent ions is that of the toxicity order given above. For certain ions, including some of those in the third heterogeneous group, the order of increasing adsorbability by charcoal is: $\text{Na} < \text{K} < \text{Ca} < \text{Zn} < \text{La} < \text{Cu} < \text{Hg} < \text{Ag}$. Adsorbability is thus seen to increase with valence, mobility, and capillary activity among the lighter elements. Among the heavier metals, electronegativity, i.e., position in the emf series, is the dominant factor in determining adsorbability. The nobler the metal the more strongly it holds its electrons, the greater it is adsorbed, and the greater is its toxicity.

When numerous physicochemical properties correlate with toxicity it is impossible to know where to lay the emphasis. All play their parts in different ways. The important point at the moment is that all correlate with the relative toxicity of the ions.

Toxicity, in the last analysis, involves an interaction between the poison and a specific component of protoplasm. Selectivity between ions and certain chemical groups is recognized. J. Northrop (*J. gen. Physiol.*, 1928, 11, 480) has shown that Cu combines primarily with the NH_2 groups of gelatin whereas La combines at some other point. Particularly important in the present discussion is the knowledge that the heavy metals, such

as Th, Ag, Pb, and to a lesser extent, La, show a pronounced tendency to form covalent bonds, especially with atoms of sulphur (FEIGL, F. *Specific and special reactions*, New York City: Elsevier, 1940).

That the correlation between toxicity and ionic properties is not limited to metallic ions but holds well for certain organic molecules, is to be seen in the perfect parallelism between the poisonous action and the molecular pattern of the barbiturates (SEIFRIZ, W. and POLLACK, H. *Arch. d. Sci. (Swiss)*, 1949, 2, 9). The highly polar sodium pentothal is the most toxic, and the weakly polar barbital the least toxic. With decreasing toxicity, the molecule becomes smaller, the carbon chains progressively shorter, and the molecule less polar.

Opposition to molecular interpretations of toxicity is not, I believe, so much a question of lack of evidence as a fear of complexity. A request for a brief account of the mechanics of kidney function was refused on the ground that the kidney has one million tubules, each functioning differently. Just what a million differences in kidney tubule activity might be I cannot imagine. Surely, there is an over-all picture of the functioning of the kidney which, taken in its entirety, presents a single mechanism. In a similar way there may be one over-all picture of the toxicity of metallic ions, with each ion possessing not so much individual characteristics as an emphasis on one property over others. The individual differences will be relative—distinctions in solubilities, equilibria, and reaction rates, determined by electron pattern and ionic behavior.

The opinion expressed above is that of the pharmacologist, A. J. Clark (*General pharmacology*, Berlin: J Springer, 1947; lithoprinted Ann Arbor, Michigan: J. W. Edwards, 1944) who says that to regard drug response as an expression of individual variation is a wholly unfruitful view. To this I should add that the surprising feature of drug action is not the variation but the clear-cut correlations. W. T. Astbury (in W. E. Clark and

P. B. Medawar [Eds.] *Essays on growth and form*, Oxford: Clarendon Press, 1945. P. 309) agrees in saying that the general shape of a molecule can often be surprisingly effective in determining certain biological reactions, "from which fact there is emerging a clearer idea of families of molecular structures." L. Pauling (*Amer. Scientist*, 1948, 36, 51) is of a similar opinion, that chemotherapeutics, enzymology, catalysis, chemical kinetics, and immunological reactions depend for their solution upon an understanding of molecular pattern. A. Szent-Györgyi (*Nature of life*, New York City: Academic Press, 1948) introduces his lecture on muscle with the statement that "Life, however varied in its appearance, is always built on the same simple principles," and he cites the similar reactions of different tissues to caffeine and veratrine.

After all, intelligent speculation involves no more than thinking about one's data, which is the way of science.

Aside from all speculation—even aside from an interpretation of data—our conclusion, reduced to its minimum irrefutable facts, forces us to concede: that it is the CO_2 molecule as such which enters cells and causes anesthesia; that we may still regard free metallic ions as responsible for the toxic effects of their salts in solution; that the poisonous action of metallic ions on the protoplasm of Myxomycetes is, in general, directly proportional to atomic weight, valence, electric charge, surface activity, adsorption, ionic diameter, hydration, mobility, and electronegativity. The present work shows the order of the toxic effects of ions on slime mold protoplasm to be the same as the order of their physical properties, certain of these properties, such as hydration and mobility, playing greater part among the lighter metals, and certain others, such as electronegativity, being dominant among the heavier noble metals.

WILLIAM SEIFRIZ

University of Pennsylvania

NEWS

and Notes

The General Advisory Committee of the AEC, headed by J. Robert Oppenheimer, has unanimously censured the O'Mahoney rider to H. R. 4177, calling for FBI investigation of all fellowship applicants (*Science*, July 28, p. 103; August 12, p. 173). The committee's statement was signed June 6 and made public August 5.

"We understand that proposals have been put forward that would require all holders of AEC fellowships to be cleared after an FBI investigation," the committee stated. "We should like to register our strong disapproval of any such procedures. Admittedly, the tensions of the times and the secret nature of the atomic energy work require elaborate checks for all who have access to classified material. But to carry over the same security concepts to holders of fellowships who will in no way have access to secret or confidential information seems to us both unwise and unnecessary."

"It is clear that these requirements of FBI investigation of prospective holders of AEC fellowships would be to extend still further the area of federal interference with the private lives of citizens. We use the word 'interference' advisedly, for it is evident that the type of questioning of friends, relatives, and acquaintances required by the investigative procedures of the FBI do constitute an encroachment on the private affairs of many people. To repeat, we grant this to be necessary in these times in those cases where persons are to be employed on secret government matters. But we are horrified by the prospects of moving this whole semi-police apparatus into the realm of youth. We believe that the reputation of many young people of the country might be . . . impaired by rumors growing out of such a system of investigation of prospective fellowship holders. Older people can

see in proper perspective calls from FBI agents, they can answer questions about acquaintances without feeling that the man being investigated is under suspicion. But young people of university age are likely to react quite differently. An atmosphere of suspicion and uncertainty is likely to be generated by the activities of federal agents among many groups of friends in colleges, universities, and in local communities. In short, the results of requiring investigations of candidates of fellowships will have serious repercussions throughout the country; it will almost certainly have a serious adverse affect on both the atmosphere of our educational institutions and the outlook of one age group of the entire nation."

About People

Luigi Crocco, of the School of Aeronautical Engineering of the University of Rome, has been appointed Goddard Professor at Princeton University, to head the Daniel and Florence Guggenheim Jet Propulsion Center established last December. Associated with Dr. Crocco will be associate professors Lester Leeds and Joseph Charyk; assistant professors Seymour Bogdanoff and Abraham Kane; and Guggenheim fellows Frank W. Bailey, Sin-I Cheng, and Frank Kreith.

Morris Edward Opler, of the Department of Sociology and Anthropology of Cornell University, has been granted a year's leave of absence to study modern developments in the villages of India. Dr. Opler's study is sponsored by the Carnegie Corporation, Cornell, the Social Science Research Council, the Viking Fund of New York, and the Watumull Foundation of Los Angeles.

Harry Davis Bruner, head of the Department of Pharmacology of the University of North Carolina Medical School, has joined the staff of the Medical Division of the Oak Ridge Institute of Nuclear Studies, where he will conduct research in cancer.

H. H. Love retired June 30 as professor and head of the Department of Plant Breeding at Cornell

University, and has been appointed professor emeritus. Dr. Love's research during his 41 years at Cornell included the development of improved varieties of small grains. **Sanford S. Atwood** will succeed Dr. Love as head of the department.

John Howard Northrop, biologist at the Rockefeller Institute for Medical Research, Princeton, New Jersey, has been appointed visiting research professor of bacteriology at the University of California, Berkeley.

Visitors to U. S.

Erik Jacobsen, head of the research department of Medicinaleo, Copenhagen, recently returned to Denmark after visiting the U. S. and Canada. Dr. Jacobsen conferred here with other investigators on the use of tetraethylthiuram disulfide ("Antabuse") in the treatment of alcoholism. Dr. Jacobsen spoke before the annual meeting of the American Psychiatric Association and a special meeting of the Association for the Advancement of Psychotherapy.

H. Bremer, of the Philips Lamp Company, Eindhoven, Holland, attended the symposium on radio wave propagation at the Naval Electronics Laboratory in San Diego. Dr. Bremer plans to be here for several weeks.

Grants and Awards

The University of Chicago has been granted \$10,000 by Swift and Company to conduct a study of sleep characteristics of infants. Children from six to twenty-six weeks of age will be observed; their movements in sleep and the distribution of periods of sleeping and wakefulness will be recorded. Special attention will be paid to the effect of diet on sleep habits.

The University of California has received a three-year grant of \$100,000 from the Rockefeller Foundation toward the establishment of an Institute of Personality Assessment and Research as an adjunct to the Department of Psychology on the Berkeley campus. The institute will

conduct basic research into the development and organization of personality through the assessment of individuals in a variety of fields and especially of persons applying for admission to professional schools of the university.

The J. Shelton Horsley Research Award of the Virginia Academy of Science has been presented to W. S. Flory, Jr., of the Blandy Experimental Farm, University of Virginia. Dr. Flory was honored for his study on pollen condition in some species and hybrids of *Rosa* with a consideration of associated phylogenetic factors.

The College of Physicians of Philadelphia awarded the **Alvarenga Prize** for 1949 to Owen Harding Wangensteen, professor of surgery, University of Minnesota, for his contributions to the etiology and therapy of gastric and duodenal ulcer. Dr. Wangensteen will deliver the Alvarenga Lecture on this subject at the college on November 2.

The Jane Coffin Childs Memorial Fund for Medical Research has announced the following appropriations totaling \$92,435 for support of cancer research projects and fellowships during the academic year 1949-50: *F. Duran-Reynals*, Bacteriology Department, Yale University School of Medicine, \$7,500 for the third year of his grant for the study of the relation of viruses to tumors; *Samuel C. Harvey*, Oncology Department, Yale University School of Medicine, \$8,500 for clinical and laboratory studies of cancer; *C. C. Little*, Roscoe B. Jackson Memorial Laboratory, \$4,500 for investigations on the mammary tumor inciter and related problems; *Eugene L. Opie*, Rockefeller Institute for Medical Research, \$8,000 for studies on osmotic and cytological effects of hepatic tumor-producing diets; *Arthur Kirschbaum*, Department of Anatomy, University of Minnesota Medical School, \$2,900 for studies on the induction and therapy of leukemia and other neoplasms of mice; *Alexander Haddow* and his associates at the Chester Beatty Research Institute of the Royal Cancer Hospital, London, \$5,000 for investigations on the

chemistry, virology, and chemotherapy of cancer; *E. S. Guzman Barron*, Biochemistry Department, University of Chicago, \$10,000 for studies of the metabolism of blood cells and of blood-producing tissues in health and disease; *T. M. Sonneborn* and *W. J. van Wagtenonk*, Zoology Department, Indiana University, \$6,500 for biochemical studies on the genetics of *Paramecium aurelia*; *Howard C. Taylor, Jr.* and *S. B. Gusberg*, Obstetrics and Gynecology Department, College of Physicians and Surgeons, Columbia University, \$4,100 for histochemical studies of abnormal growth of the human uterus; *Sir Ernest L. Kenaway*, St. Bartholomew's Hospital, London, \$1,500 for statistical and laboratory studies of cancer; *Edward W. Shrigley*, Microbiology Department, Indiana University Medical Center, \$4,000 for studies on the biology of the Rous sarcoma virus and of the properties of experimentally induced tumors; *Frances L. Haven*, Biochemistry Department, University of Rochester School of Medicine and Dentistry, \$3,000 for studies on the selective localization of radioactive estrogens and allied substances in normal and cancer-bearing tissues; *Rivka Ashbel*, Department of Surgery, Harvard Medical School, \$2,500 for completion of a specific histochemical method for the demonstration of adrenal cortical ketosteroid; *Nathan B. Friedman*, Division of Laboratories, Cedars of Lebanon Hospital, Los Angeles, \$2,735 for studies on cellular dynamics in intestinal mucosa as determined with antimitotic agents on animals of different age and nutritional status; *Joseph E. Sokal*, Department of Pathology, Yale University School of Medicine, under guidance of *C. N. H. Long* and *H. S. N. Greene*, \$2,500 for the third year of his fellowship; *John J. Trentin*, Department of Anatomy, Yale University School of Medicine, under guidance of *William U. Gardner*, \$4,400; *Walter S. McNutt*, University of Copenhagen, under guidance of *E. Hoff Jorgensen* and *H. Kalckar*, \$3,000.

The Louis Edward Levy Medal of the Franklin Institute of Pennsyl-

vania was awarded to *Alan S. Fitzgerald*, electrical research engineer of San Francisco, for his work on the design criteria of nonelectronic amplifiers.

Colleges and Universities

The University of Michigan and the Mt. Wilson Observatory are cooperating in a solar research project whose immediate object is obtaining a complete record of the infrared spectrum, to be made available as an atlas for working astronomers. An infrared spectrometer, contributed for the purpose by the Office of Naval Research, has been installed on a solar telescope at the observatory. Two long range studies are also planned, to supplement and check solar observations at the university's McMath-Hulbert Observatory. One is a determination of the abundance, varieties, and temperatures of such compounds in the earth's atmosphere as carbon dioxide, nitrous oxide, and methane, and the other is a study of the structure of the solar atmosphere.

Wayne University, Detroit, will receive a differential analyzer and cinema integrator as a gift from the Massachusetts Institute of Technology. MIT is acquiring a machine of newer design, and will no longer need the earlier one, which was designed by Vannevar Bush before the war and has since been remodeled.

A new agricultural experiment station will be established at **Virginia Polytechnic Institute** as the result of a gift from Paul Mellon of a 420-acre farm and \$125,000 for its operation. The station will be used to develop pasture and forage crops for northern Virginia.

Industrial Laboratories

The Linde Air Products Company, unit of Union Carbide and Carbon Corporation, has announced the synthesis of clear crystals of cadmium tungstate, which is being considered for use as a phosphor in scintillation counters for the detection of high energy radiations. This new tungstate maintains high phosphor effi-

ciency throughout the temperature range of 0° to 75° C and has high physical and chemical stability. The synthetic crystals are now available in $\frac{1}{8}$ -inch square section rods, in lengths up to 2 inches. In special cases larger single pieces can be supplied.

Eastman Kodak Company is producing photographic emulsions for nuclear research in pellicle form, without the usual glass support. In this form emulsions can be as thick as 250 microns and still be developed evenly because developing solutions work on both sides.

Meetings and Elections

Britain, which produces the largest amount of manufactured gas in the world, was appropriately the venue for the **4th International Gas Conference**, which was held June 15-17. The conference, organized by the International Gas Union, met for the first time since the war. An address of welcome was made by Hugh Gaitskell, Minister of Fuel and Power. President of the conference was C. M. Croft, of the British Institution of Gas Engineers, who retired toward the close of proceedings in favor of M. Brabant of Brussels, president of the union for the next three years.

Object of the International Union is the promotion of international cooperation in fuel research and technology. The organizers were glad to welcome delegates and visitors from Austria, Belgium, Canada, Czechoslovakia, Denmark, France, Great Britain, Holland, Italy, Norway, Sweden, Switzerland, Turkey, and the U. S. No curtain divides this body, which is essentially technical and not concerned with political or labor matters.

Principal themes were improvement of the efficiency of industrial gas manufacture and domestic utilization, which many countries reported to be the principal one. H. Zollkofer, general secretary of the International Gas Union and the Swiss Society of the Gas and Water Industry, pointed out, for instance, that in Switzerland about 80 percent of gas distributed is consumed domestically. Papers on the design of domestic burners were therefore a

feature of the conference. There was also a valuable survey by A. R. Bennett of progress in the domestic utilization of gas brought about by radiation, heat transfer, and aerodynamic studies. Reviews of research in France, Britain, and the U. S. were presented. Two of the British papers discussed procedures adopted for maintaining gas supplies during bombing of mains.

There were three papers of chemical interest. J. E. Carrière, of Holland, discussed modern methods of protecting cast iron and steel pipes, including the use of blown asphalt bitumen with fillers. A project for absorption and recovery of carbon monoxide from town's gas was presented by H. Deringer of Wintertour. More elaborate was the paper by P. Ferrero of Belgium on the chemical "valorization" of coal gas to yield ethylene derivatives (notably glycols) by fractionating the original gas for its 2 percent of this valuable olefine.

Important among the many visits which contributed to the success of the meeting was a tour of the highly mechanized Beckton Gas Works, which consumes $1\frac{1}{4}$ million tons of coal and produces 22,600 million cubic feet of gas annually. Major gas consumers were also visited.

I. BERKOVITCH

The 19th International Congress of Americanists will be held in New York City September 5-12. The congress, which meets biennially, has as its objective the historic and scientific study of the two Americas and their inhabitants. The Viking Fund, Inc. is sponsoring the meetings and the American Anthropological Association is acting as principal host.

The Third National Congress of Fruit Growing will be held in Ferrara, Italy, October 9-16. Scientists and technicians throughout the world are invited to attend. Additional information may be obtained by writing to the Secretary of the Third National Congress of Fruit Growing, Foreign Section, Via Salita Castello 10, Ferrara, Italy.

The American Standards Association will hold its thirty-first annual meeting October 11-14 at the Waldorf-Astoria Hotel in New York.

The National Academy of Sciences will hold its autumn meeting at the University of Rochester, Rochester, New York, October 24-26.

The Seventh Annual Pittsburgh Conference on X-Ray and Electron Diffraction will be held November 7-8 at the Mellon Institute of Industrial Research, Pittsburgh.

The Illinois Institute of Technology chapter of Sigma Xi elected the following officers for 1949-50: president, Karl Menger of the Department of Mathematics; vice-president, Eric T. B. Gross of the Department of Electrical Engineering.

Deaths

John R. Carty, 56, former professor of radiology and chief of the X-Ray Department of the New York Hospital, Cornell Medical Center, died July 12. Dr. Carty had retired several years ago because of ill health.

Alfred Rehder, 85, professor emeritus of the Arnold Arboretum, Harvard University, died July 21. Dr. Rehder conducted research in the taxonomy and bibliography of woody and Chinese ligneous plants.

Archie Garfield Worthing, 68, professor of physics at the University of Pittsburgh, died July 30. Dr. Worthing had done considerable work in high temperature measurements and tungsten research. He was past president of the Optical Society of America and of the American Association of Physics Teachers, and a member of the executive board of the American Institute of Physics.

Hyman H. Goldsmith, 42, physicist and chief of the Information and Publication Divisions of the Brookhaven National Laboratory at Upton, Long Island, died August 7 as the result of a swimming accident. Dr. Goldsmith was formerly associated with the Manhattan District Project and was co-editor of the *Bulletin of the Atomic Scientists*, published by the Educational Foundation for Nuclear Research.

Edward Lee Thorndike, 74, professor emeritus of educational psychology at the Teachers College of

Columbia University, where he had been a staff member since 1899, died August 9 at his home in Montrose, New York. Dr. Thorndike was one of the first to devise tests for the measurement of reasoning and learning ability; his Alpha test, used in World War I, introduced the present Army classification system.

Homer Adkins, 57, professor of chemistry at the University of Wisconsin, died August 10 at his home in Madison. Professor Adkins' most recent research was concerned with reactions of hydrogen and organic compounds in the presence of various catalytic agents. Outside the field of catalysis he had contributed greatly to knowledge of the reactivity of a variety of organic types.

Science has received word that the **Peiping Union Medical College** is continuing its teaching and research program, unaffected by the change in government. The city was besieged for a period of six weeks in December and January and after skirmishes in the suburbs, the Chinese Communist army took possession of the city. There was no extensive destruction of property and only a small number of casualties in the municipal area. Municipal power and light were curtailed over this period; but the college maintains its own power plant, and during the siege classes continued without interruption. American staff members have remained at their posts.

Following the turnover, postal communication was interrupted for almost two months, but this has now been restored. Surface mails during the winter were greatly delayed and journals for the library for the past six months are just now being delivered.

The college was occupied by the Japanese military during World War II and the first postwar entering class in medicine was received in 1947. The rehabilitation program is about half accomplished; more departments are to be restaffed this year and additional wards in the hospital put into service.

Unesco proposes to publish later in the year a **manual on the inter-**

national exchange of publications. The manual will include an appendix containing a classified list of institutions, including libraries, universities, scientific institutions, learned societies, etc. throughout the world, which are willing to exchange either their own publications or other publications which they have regularly at their disposal. All institutions which have so far not sent to Unesco details of their exchange material in one form or another are urged immediately to communicate the following information to the Unesco Clearing House for Publications, 19 Avenue Kléber, Paris, 16^e: (a) Name and full address of institution. (b) Exact titles of publications offered. (c) Institutions which wish to exchange their publications only under certain conditions are asked to state what these conditions are. Only information which reaches Unesco before *October 1st* can be used in the manual.

The **Sectional Committee on Standardization of Optics of the American Standards Association** recently held its second meeting. Subcommittees reported completion of proposed standards on nomenclature and specifications of color, and research on light sources. The committee is sponsored by the Optical Society of America.

The **National Registry of Rare Chemicals**, 35 West 33rd Street, Chicago 16, Illinois, has submitted the following list of wanted chemicals: pentamethylphenol, durenol, 8-chlorotheophylline, 2-amino-1,3,4-triazole, vanillyl amide (Δ^2 -nonenoate), phosphonium bromide, 5-hydroxyuracil, perfluoroethylcyclohexane, vicine, myristicine, absinthin, 7-hydroxy-1-H-v-triazolo-(d)-pyrimidine, 7-(α)-12-(α)-dihydroxyprogesterone, 12-(α)-hydroxyprogesterone, bis-(2-(2'-fluoroethoxy)-ethoxy)-methane, xanthotoxin, sodium pregnanediol glucuronate, phloretin, hemipic acid, *p*-fluoroaniline, erythrophleine, and cyanogen.

An International Bibliography on Atomic Energy has been prepared by the Atomic Energy Commission group of the Department of Security Council Affairs of the United Na-

tions Secretariat. Volume I, which is now available, is a selective bibliography of material on the political, scientific, and social aspects of atomic energy. Volume II, which will be published later this year, will discuss published scientific literature on atomic energy.

The **1947-48 Report of the Committee on the Measurement of Geologic Time** has just been published. The report includes an obituary on Alfred Church Lane; a summary of the committee's activities during the year; a report from Arthur Holms, of the University of Edinburgh; an article on "The Necessity for Different Values for the Ratio Pb/V of the Crust and the Rest of the Planet," by Juan Manuel Lopez de Azcona (translated by A. H. and J. P. Marble); a review of work in Japan by Dr. Marble; "Archaeological Ages by Natural Radiocarbon Content," by W. F. Libby, with comments by R. F. Flint; "Preliminary Report on Determining the Age of Rocks by the Lead-Uranium Ratio of Zircon, Apatite, and Sphene from the Rocks Using Alpha Counting and Spectrographic Methods," by E. S. Larsen, Jr., N. B. Keevil, and H. C. Harrison; and an annotated bibliography of articles relating to the measurement of geologic time, compiled by Dr. Marble. The report may be obtained from the Division of Geology and Geography, National Research Council, 2101 Constitution Avenue, N.W., Washington 25, D. C., at \$1.00 a copy.

Make Plans for—

Aeromedical Association, 20th annual convention, August 29-September 1, Statler Hotel, New York City.

American Mathematical Society, August 30-September 2, 55th summer meeting in conjunction with summer meetings of **Econometric Society**, **Institute of Mathematical Statistics**, and **Mathematical Association of America**, University of Colorado, Boulder.

American Psychological Association, September 6-10, Shirley Savoy Hotel, Denver, Colorado.